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# THE LANCET

No. 7003 LONDON SATURDAY 16 NOVEMBER 1957 VOL. II FOR 1957


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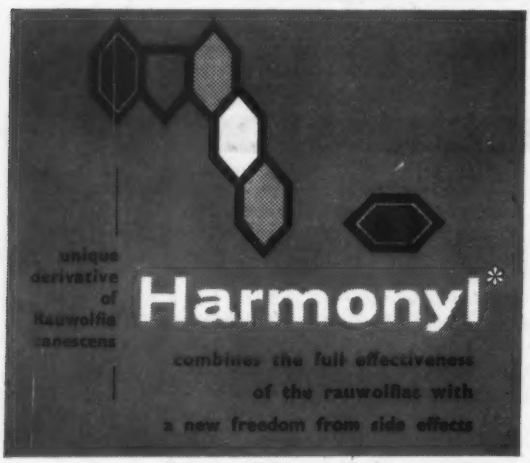
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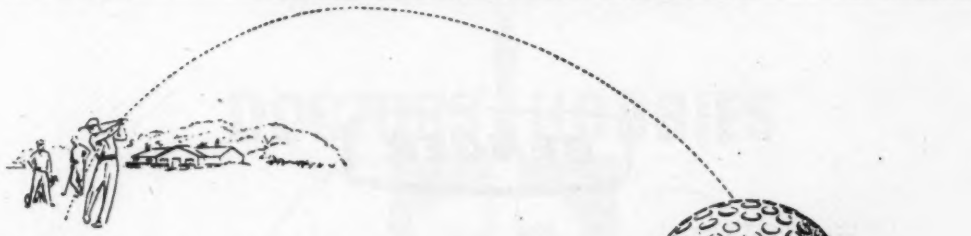

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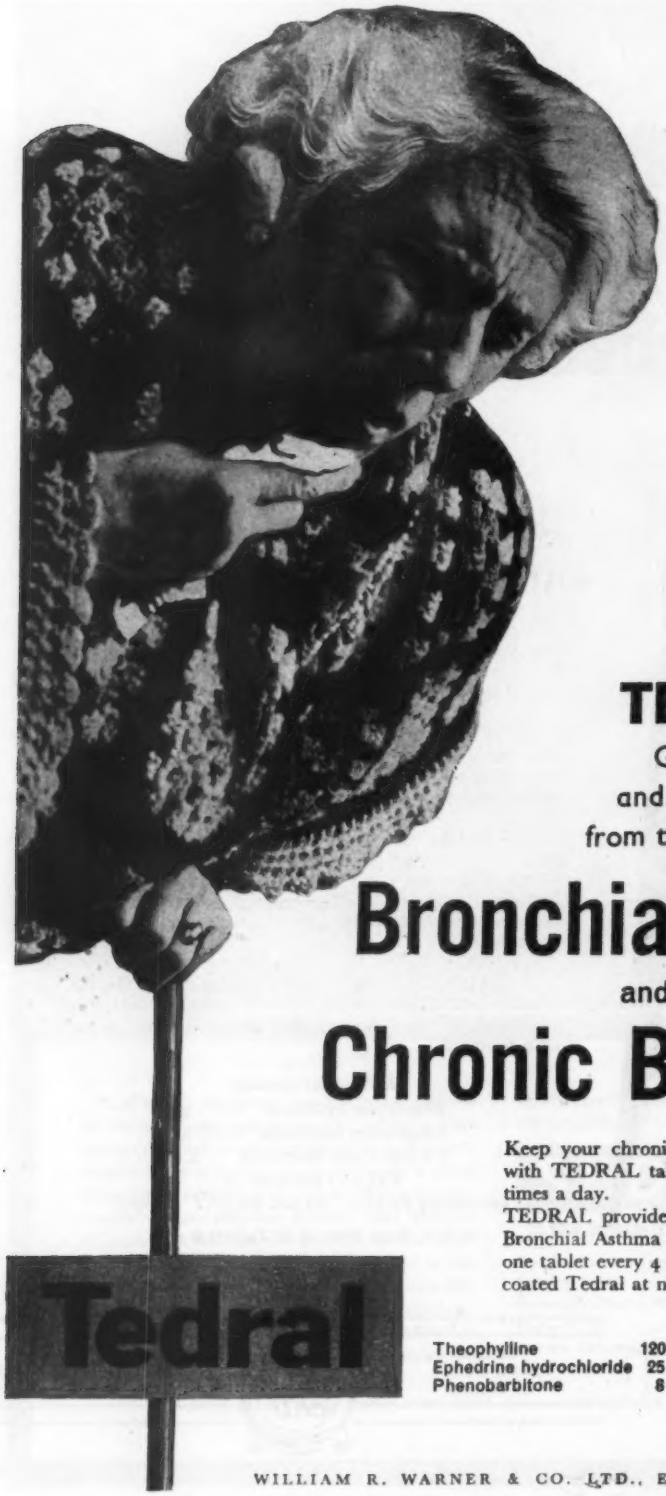
Dispensing Packs of 250 and 500 (*P.T. exempt*).

*N.H.S. Basic Price of 50 Tablets is 1/5½.*

Sample and literature on request.

A. WANDER LTD.,
42 Upper Grosvenor Street,
London W.1.

M.398




# TEDRAL
TRADE MARK

Gives rapid
and lasting relief
from the symptoms of

# Bronchial Asthma
and
# Chronic Bronchitis

Keep your chronic bronchitic patients up and about with TEDRAL taken prophylactically one tablet four times a day.

TEDRAL provides 24 hours protection to your aged Bronchial Asthma and Chronic Bronchitic patients with one tablet every 4 hours during the day and one enteric coated Tedral at night.

| | |
|---|---|
| Theophylline | 120 mg. (2 gr.) |
| Ephedrine hydrochloride | 25 mg. (½ gr.) |
| Phenobarbitone | 8 mg. (⅛ gr.) |

WILLIAM R. WARNER & CO. LTD., EASTLEIGH, HAMPSHIRE.

TED 204/4

# as the patient sees it . . .

The ophthalmic forms of ACHROMYCIN tetracycline are acceptable in *every* sense —not only from the physician's angle but from the patient's viewpoint too. Simple and painless to use, they are virtually free from unwanted side effects. The patient will therefore co-operate to the full in following the course of treatment prescribed.

In many cases of conjunctivitis and of ocular infection due to staphylococci, streptococci and other sensitive organisms, *local* measures with the Ophthalmic Ointment or Sterilized Powder are fully effective. In more severe conditions, however, simultaneous systemic treatment should be adopted with one of the oral forms of the drug.

# Achromycin*

TETRACYCLINE

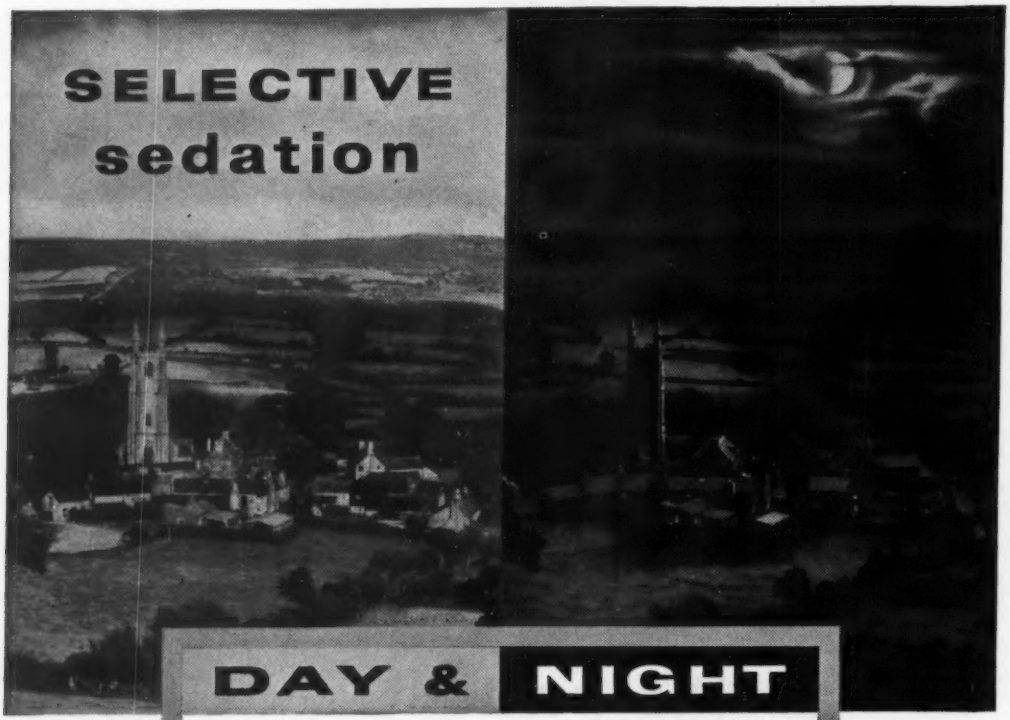
*Regd. Trade Mark

**Ointment (Ophthalmic) 1%:**
10 mg. per Gm.: ¼-oz. tubes in boxes of six

**Ophthalmic Powder Sterilized:**
25 mg. per vial: supplied with dropper vial

CYANAMID 1907 50 1957

LEDERLE LABORATORIES DIVISION
*Cyanamid* OF GREAT BRITAIN LTD., London W.C.2




DAY & NIGHT

For each individual patient who is in need of sedation or hypnosis, there is a LILLY barbiturate that meets the requirements exactly.

**'Seconal Sodium'** When rapid action yet brief duration is called for.

**'Sodium Amytal'** For routine sedation in the anxiety case.

**'Tuinal'** In the chronic insomnia case.

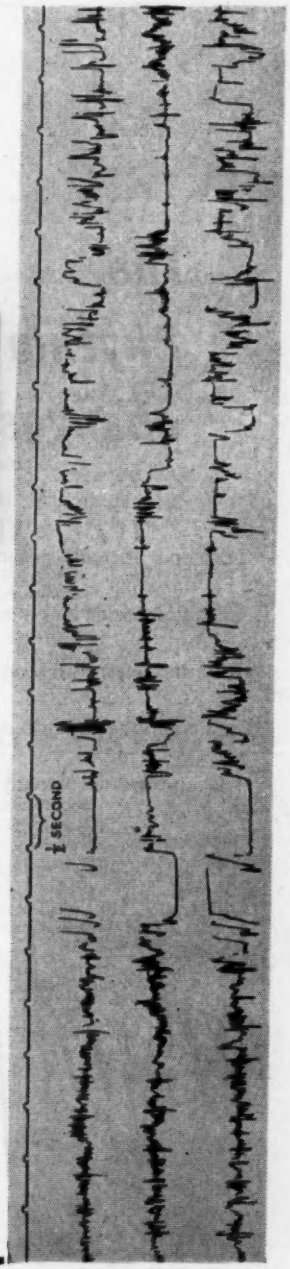
**'Amytal'** Sedation in the hypertensive, peptic ulcer, skin or cardiac case.

*Let it be a Lilly barbiturate*

14 ELI LILLY AND COMPANY LIMITED, BASINGSTOKE, ENGLAND

# A NEW Therapy in EPILEPSY

# Trinuride




| | |
|---|---|
| *Phenylethylacetylurea* | *0·200g* |
| *Diphenyl Hydantoin* | *0·040g* |
| *Phenobarbitone* | *0·015g* |

## ADVANTAGES

Efficient and reliable control of fits, together with improved mental alertness, which enables the epileptic patient to take a normal place in social life.

## TOXICITY

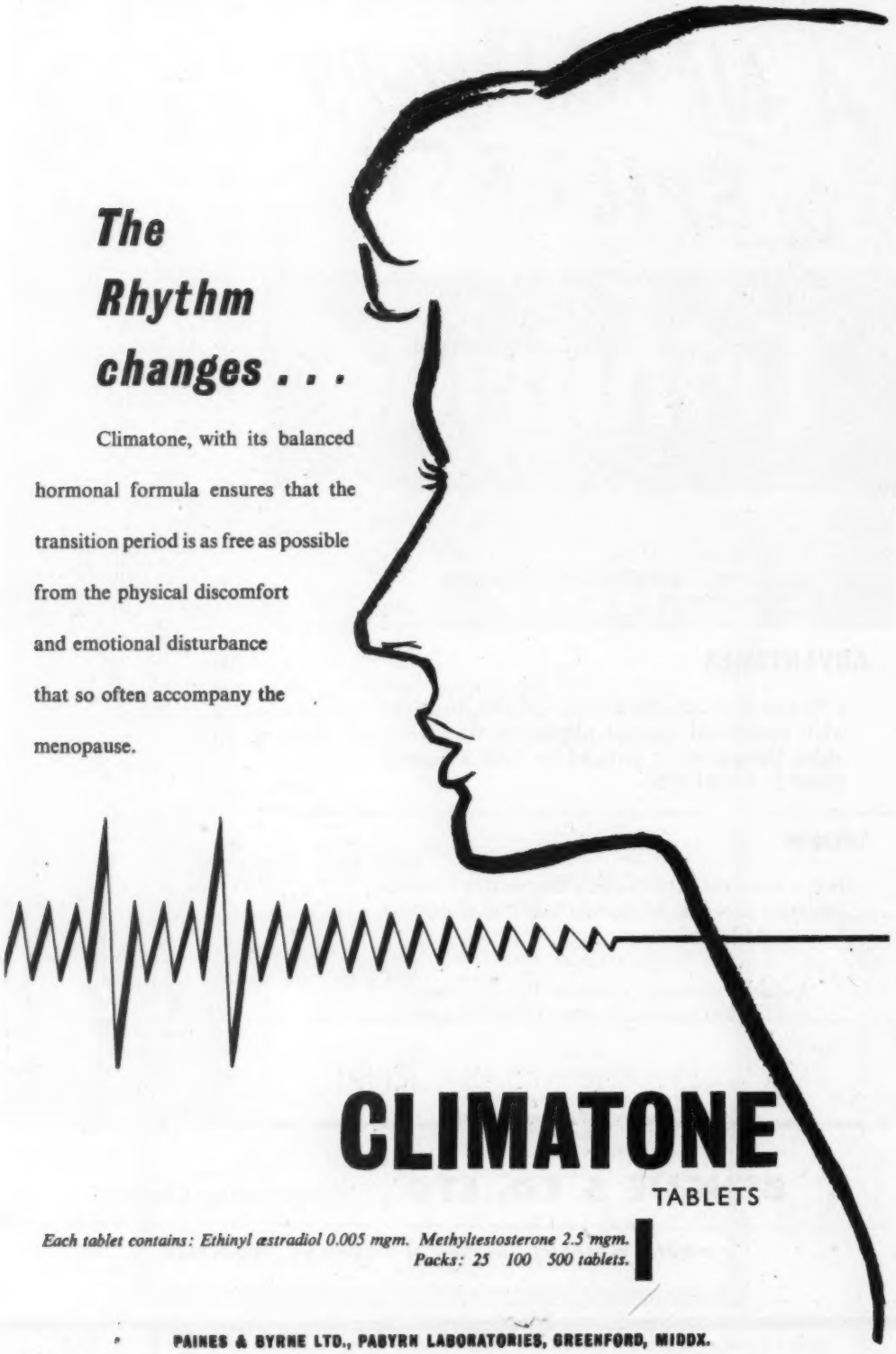
In extensive clinical trials over a long period, Trinuride has been found to be singularly devoid of toxicity.

*Requisite quantities available free of charge to Clinicians wishing to conduct Hospital trials*

*Literature and abstracts available on request.*

**BENGUE & CO. LTD.,** *Manufacturing Chemists.*

MOUNT PLEASANT · ALPERTON · WEMBLEY · MIDDLESEX



# *The Rhythm changes . . .*

Climatone, with its balanced hormonal formula ensures that the transition period is as free as possible from the physical discomfort and emotional disturbance that so often accompany the menopause.

# CLIMATONE

TABLETS

*Each tablet contains: Ethinyl æstradiol 0.005 mgm. Methyltestosterone 2.5 mgm.*
*Packs: 25 100 500 tablets.*

**PAINES & BYRNE LTD., PABYRN LABORATORIES, GREENFORD, MIDDX.**

# *'An Anginal Patient— but not an invalid!'*

**Successful treatment of angina pectoris should enable the patient to recover confidence in his ability to work.**

## 'PENTOXYLON'

**can help to achieve this happy result**

## 'PENTOXYLON'

tablets contain 10 mg. P.E.T.N. (pentaerythrityl tetranitrate), a potent coronary vasodilator, and 1 mg. 'Rauwiloid', an alkaloidal fraction of *Rauwolfia serpentina.*

## 'PENTOXYLON'

removes the dread of another attack, and increases exercise tolerance. The need for nitroglycerin is greatly reduced when 'Pentoxylon' is used prophylactically, and in hypertensive patients there is a reduction in blood pressure.

**DOSAGE:** *1 or 2 tablets four times daily* before *meals.*

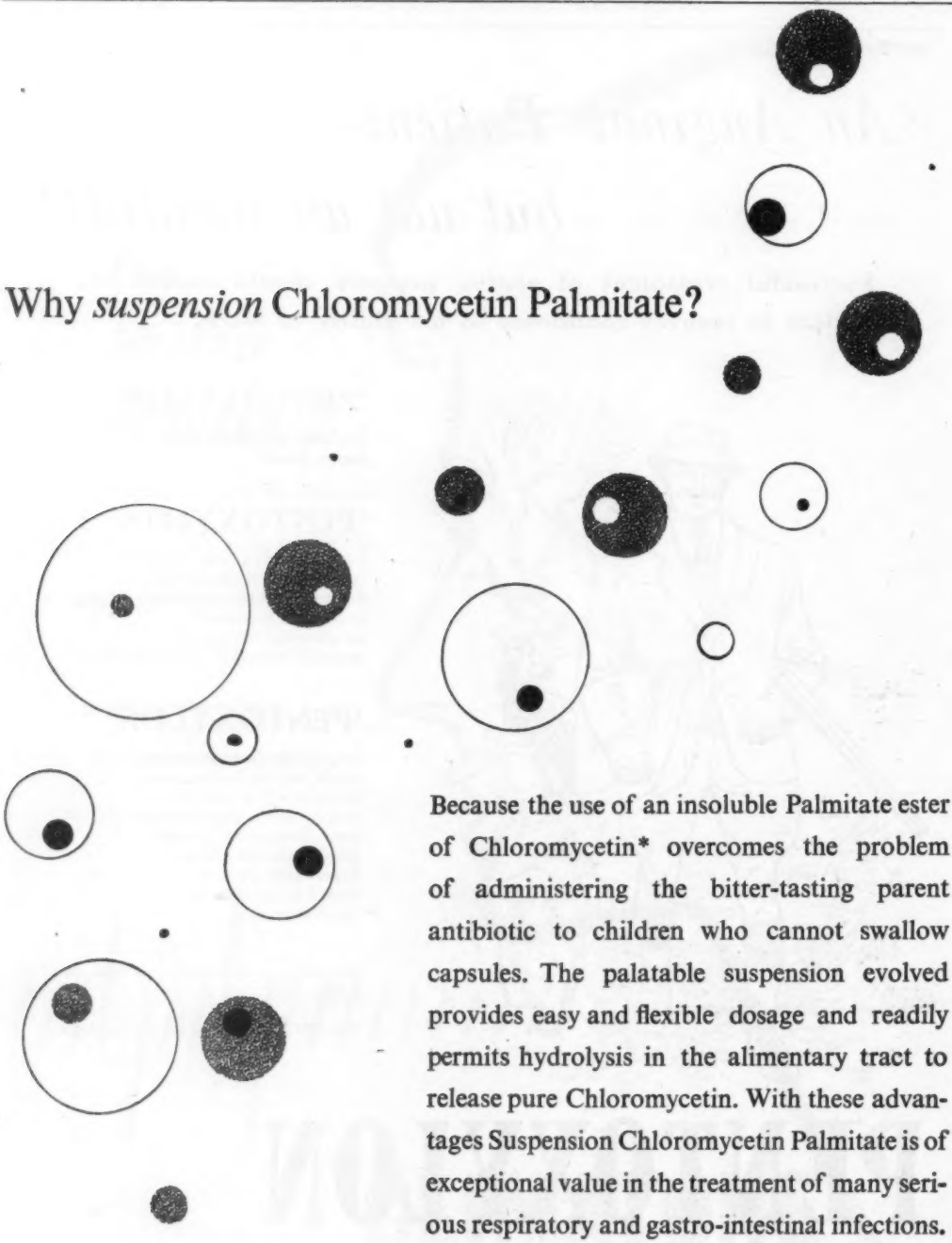
**PACKS:** *Bottles of 25, 100 and 500 tablets.*

# PENTOXYLON

RIKER

*'Pentoxylon' and 'Rauwiloid' are registered trade marks. Regd. Users:*
RIKER LABORATORIES LIMITED · LOUGHBOROUGH · LEICS.

# Why *suspension* Chloromycetin Palmitate?



Because the use of an insoluble Palmitate ester of Chloromycetin* overcomes the problem of administering the bitter-tasting parent antibiotic to children who cannot swallow capsules. The palatable suspension evolved provides easy and flexible dosage and readily permits hydrolysis in the alimentary tract to release pure Chloromycetin. With these advantages Suspension Chloromycetin Palmitate is of exceptional value in the treatment of many serious respiratory and gastro-intestinal infections.

* TRADE MARK

**SUSPENSION CHLOROMYCETIN PALMITATE**

BOTTLES OF 60 ML.

PARKE, DAVIS & COMPANY LTD. (Inc. U.S.A.) HOUNSLOW, MIDDX. Tel: Hounslow 2361

116

**Whichever way you take it . . .**

**BY MOUTH** *as most patients do*

**BY RECTUM** *when there is severe nausea and vomiting early in the attack*

# Cafergot

BY **SANDOZ**

**aborts the attack of migraine in more than 80% of cases**

TABLETS — 1 mg. Ergotamine Tartrate B.P.
100 mg. Caffeine B.P.

SUPPOSITORIES — 2 mg. Ergotamine Tartrate B.P.
100 mg. Caffeine B.P.
0.25 mg. total alkaloids of belladonna
100 mg. isobutylallyl barbituric acid

**Sandoz Products Limited**

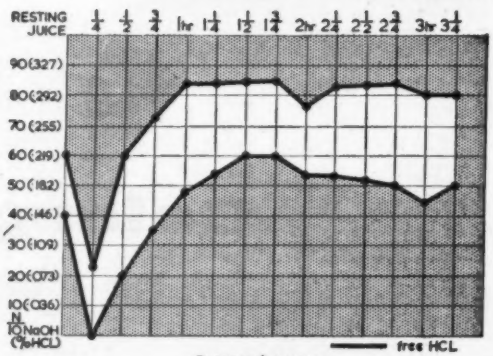
**Sandoz House**
**23 Great Castle Street**
**London, W.1**

"an approach to the ideal is provided by a slowly dissolving antacid tablet which is lodged between the gum and cheek. Thus, with each act of swallowing, alkali is carried down over the gullet to the stomach. It is remarkable how little is the quantity needed to depress effectively the concentration (pH) of gastric HCl. The first such tablet ('nulacin')...."

*Practitioner*, January, 1957.

# NULACIN THERAPY

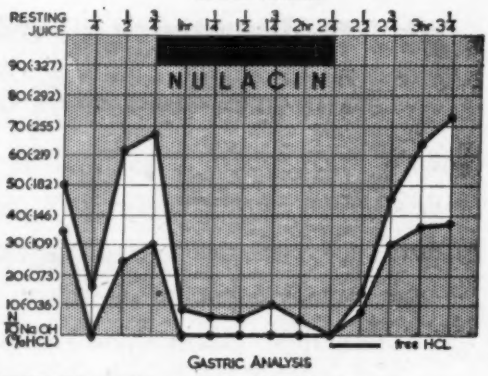
## —Simple, safe, effective




GASTRIC ANALYSIS

A Nulacin tablet effectively depresses the concentration of gastric HCl in peptic ulcer and other conditions of hyperacidity. It also provides protection against gastric HCl to the otherwise unprotected oesophageal wall and in such conditions as oesophagitis and hiatus hernia.

SUPPLY. Nulacin tablets may be prescribed on E.C.10. The dispensing pack of 25 tablets is free of Purchase Tax. (Basic price to N.H.S.: 2/-). Also available in tubes of 12.




GASTRIC ANALYSIS

**HORLICKS LIMITED** *Pharmaceutical Division, Slough, Bucks., England*

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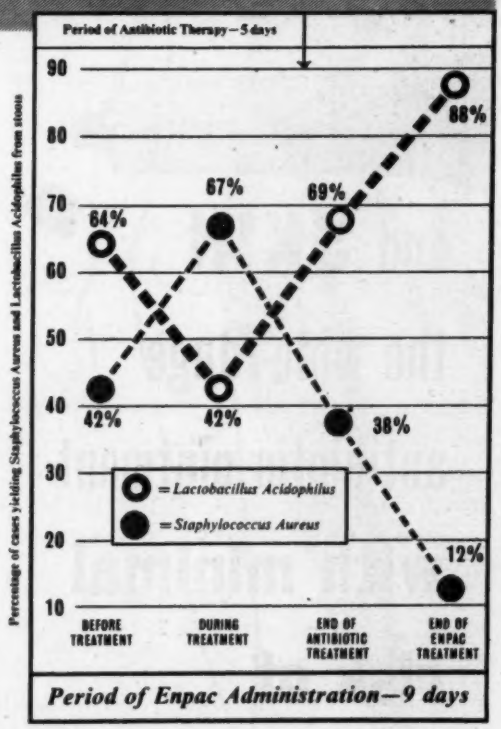
Medical Treatment of Peptic Ulcer, *Med. Press*, 27th February, 1952, **227**: 195-199

The Control of Gastric Acidity, *Brit. Med. J.*, 26th July, 1952, **2**: 180-182

# The effect of ENPAC on Intestinal Flora during Antibiotic Therapy

This graph illustrates the striking result of a clinical trial with 66 patients at Bristol recently published in the *Lancet*. It demonstrated how during antibiotic treatment *Enpac* builds up resistant lactobacilli while reducing the number of staphylococci to a low level. By contrast, *when the antibiotic was used alone*, lactobacilli dropped to the low figure of 16%, whereas resistant staphylococci flourished greatly at the high level of 76%.




## SUMMARY

*Extract from the Lancet article on the Bristol clinical trial*

"It was found that the staphylococci increased in both groups at the beginning of antibiotic therapy. Staphylococci continued to increase in the patients taking the antibiotic alone, but in those taking Enpac there was a pronounced drop in numbers following the initial rise. Simultaneously, in this latter group the lactobacilli were rapidly established and continued to multiply. This followed the elimination of the normally non-resistant lactobacilli by the antibiotic during the early days of treatment."
(*Lancet*, 1957, i, 899)

*Samples and literature are freely available to the medical profession on request.*

Enpac REGD TRADE MARK

**LLOYD-HAMOL LTD.** Sole Distributors,
11, Waterloo Place, London, S.W.1

*A British product developed by Aplin & Barrett, Ltd., Biologicals Division.*

# NEOBACRIN

TRADE MARK

for **EYE**

and **SKIN**

## the wide-range antibiotic ointment with minimal risk of sensitisation

THIS CHART shows the wide range of gram-positive and gram-negative organisms jointly covered by neomycin and bacitracin. Combined in Neobacrin, both antibiotics in most cases are lethal to the bacteria, not merely inhibitory.

| Gram-Negative Organisms | Bacitracin | Neomycin |
|---|---|---|
| Aerobacter aerogenes | R | S |
| Klebsiella pneumoniae | R | S |
| Neisseria gonorrhoeae | S | R |
| Proteus vulgaris | R | S |
| Pseudomonas aeruginosa | R | S |

| Gram-Positive Organisms | Bacitracin | Neomycin |
|---|---|---|
| Clostridium perfringens | S | R |
| Clostridium sporogenes | S | R |
| Corynebacterium diphtheriae | S | S |
| Corynebacterium diphtheroides | S | S |
| Diplococcus pneumoniae | S | MS |
| Staphylococcus albus | S | S |
| Staphylococcus aureus | S | S |
| Streptococcus pyogenes | S | MS |
| Streptococcus viridans | S | MS |

KEY: S—Sensitive, MS—Moderately sensitive, R—Resistant. All sensitivities may be increased by the synergistic action of both agents.

In every way Neobacrin is the antibiotic ointment of choice for everyday treatment of common skin and eye infections. The most important reason why it is so useful is that neither of its component antibiotics is likely to cause sensitisation; a distinct possibility with many of the antibiotics that are used systemically as well as locally.

**INDICATIONS**

Skin Conditions
- Impetigo
- Sycosis barbae
- Furunculosis
- Secondarily infected wounds, burns, ulcers
- Infectious eczematoid and pyogenic dermatitis

Superficial Infections of the Eye
- Conjunctivitis
- Blepharitis
- Infected Meibomian glands or lachrymal sacs

**PRESENTATION**

15 gm. tube
3½ gm. tube (with ophthalmic nozzle)

Each gram of NEOBACRIN contains 5 mg. neomycin sulphate and 500 units zinc bacitracin in bland paraffin base.

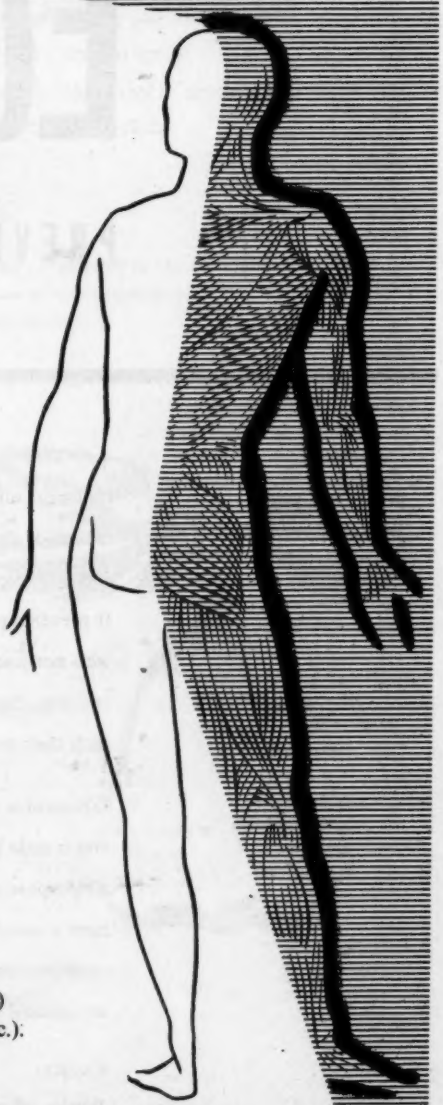
Glaxo Laboratories Ltd., Greenford, Middlesex. BYRon 3434

GLAXO

*Subsidiary Companies or Agents in most countries*

*NEW*

# Protein Tissue Building without Virilisation



Nilevar* represents a major advance in therapy. No significant virilisation accompanies its potent nitrogen-retaining action when given in full therapeutic dosage. Patients quickly regain appetite and weight and feel better in themselves. Nilevar can be given to patients

**irrespective of age or sex**
**in simple daily doses**
**for as long as it is therapeutically needed**

**INDICATIONS:**

Convalescence from acute illness
Chronic wasting diseases
Malnutrition
Recovery after surgery
Preparation for planned surgery
Recovery phase of severe burns and traumata
For weight increase after premature birth

Nilevar is available in bottles of 25 and 50 tablets (10mg.) and in boxes of 6 ampoules (each containing 25 mg. in 1 c.c.).

*Literature available on request*

**Nilevar**

*brand of norethandrolone*

**Registered Trade Mark*

SEARLE HIGH WYCOMBE, BUCKS. Tel: High Wycombe 1770

NV: PI07

# Equaprin*

## PREVENTS PAIN

Equaprin offers a unique approach towards the ideal analgesic for the control of chronic pain that may arise in conditions such as tension states, menstrual disorders, influenza and rheumatoid arthritis. It prevents pain from reaching troublesome proportions by dealing with not just the somatic but also with the psychological aspects of the problem, thus enabling your patients to face up to continuing with their normal mode of life.

Equaprin is a logical combination of the safe, selective sedative and muscle relaxant, meprobamate, with that re-established and accepted all-purpose analgesic, aspirin. Used together, both compounds have a complementary action, and preliminary clinical observations confirm that *Equaprin is more effective in more cases* than either constituent used alone.

PACKS:

Bottles of 20 and 250 tablets. Each tablet contains 125 mg. meprobamate enclosed in a shell of 400 mg. acetylsalicylic acid.

Detailed information is available and will be supplied on request.

Wyeth

**trade mark*

JOHN WYETH & BROTHER LIMITED,
CLIFTON HOUSE, EUSTON ROAD, LONDON, N.W.1
Eqp.1

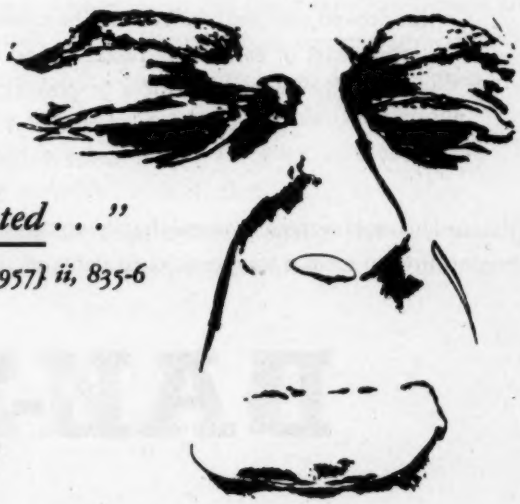
## the basic problem

*"Apart from the impossibility of testing the antibiotic-sensitivity of the bacterial flora of more than a small fraction of the affected population, the onset of pneumonia may be so sudden and catastrophic that immediate chemotherapy is essential . . ."* †

## one name

*". . . the real dilemma . . . whether to aim the attack primarily against* H. influenzae, *using the tetracyclines or chloramphenicol, or against* Staph. aureus *with erythromycin or novobiocin."* †

In a single preparation Sigmamycin answers this dilemma. It is rapidly effective against *both* these organisms.



*". . . patients may die within twenty-four hours if not effectively treated . . ."*

*"Bacteria and Influenza"* † *Lancet {1957} ii, 835-6*

## the only one name

*". . . the best course may be to use a combination of antibiotics from both groups . . ."* †

(The broad and medium spectrums)

Sigmamycin, which contains tetracycline and oleandomycin, is the *only* preparation currently available in this country which meets this description in a single preparation.

## the complete answer

# sigmamycin*

oleandomycin tetracycline

Pfizer PFIZER PHARMACEUTICALS. MANUFACTURED AT SANDWICH AND PROCESSED AT FOLKESTONE, KENT. ★ Registered Trade Mark

# TWO NEW PRODUCTS

## I *A derivative of natural vitamin E*

Most single vitamins have been available to the profession for many years in forms acceptable as pharmaceutical preparations.

Vitamin E has presented difficulties. Natural sources, e.g. wheat germ and wheat germ oil, do not contain high enough concentrations: synthetic vitamin E, while useful, has not proved uniformly effective. The chemistry of vitamin E has now been elucidated after years of exhaustive research and the active insomers are known. It has thus become possible to present tablets of stable, high activity in the form of dextro-alpha tocopheryl succinate, derived from natural vitamin E. Each tablet of 200 mg. has an activity of 242 i.u. vitamin E.

This achievement means that Vitamins Limited can now offer to the profession a preparation to meet a long-continued demand.

# DAL-TOCOL

The wide distribution of vitamin E in the body suggests a fundamental biochemical function and this would seem to be in relation to the metabolism of protein both in cellular and muscular organs. The most hopeful therapeutic approach is in relation to disease of the coronary and peripheral arteries, in fibrosis of skeletal muscle and in maintaining functional cellular integrity. Clinical trials have led to divergent results and to controversial issues. It is hoped that the use of an acceptable preparation of uniform strength and high concentration will provide evidence which will help to clear up some of the doubts and uncertainties associated with vitamin E treatment.

**PACKS:** Tablets in packs of 100 and 500

*

**See our Stand No. 43 at the London Medical Exhibition or write for details to:**

# FROM VITAMINS LIMITED

## 2 *Modified Phenobarbitone Therapy*

SEDATION WITHOUT DEPRESSION

TROPENAL is a combination of phenobarbitone with vitamins of the B complex and vitamin C. Its formula has been designed to take advantage of the fact that many of the side-effects of barbiturates are inhibited by the simultaneous administration of generous doses of these vitamins. Phenobarbitone is excreted only slowly, continued administration causing tissue retention. As the drug is slowly released from this tissue reservoir there is an increasing risk of toxic side-effects unless there is a concomitant high concentration of the necessary vitamins. By judicious combination it becomes possible to prescribe phenobarbitone for those conditions in which it is properly indicated for prolonged periods without the development of depression, headache and tremor which are such common features of long-continued treatment. (Skin sensitivity is unaffected.)

**The commoner indications for Tropenal are thus: epilepsy, anxiety states, especially those accompanied by insomnia and restlessness, and alcohol withdrawal.**

# TROPENAL

**FORMULA:**

*Each tablet contains:*

| | | |
|---|---|---|
| Aneurine hydrochloride | B.P. | 5 mg. |
| riboflavine | B.P. | 5 mg. |
| pyridoxine | B.P.C. | 2 mg. |
| nicotinamide | B.P. | 15 mg. |
| ascorbic acid | B.P. | 50 mg. |
| phenobarbitone | B.P. | 16 mg. (¼ gr.) |

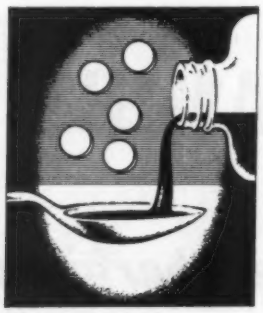
**DOSAGE**

One to four tablets daily

**PACKS**

Tablets in packs of 100 and 500

**VITAMINS LIMITED** UPPER MALL, LONDON, W.6.



# BUFFERED THEOPHYLLINE FOR THE PROPHYLAXIS & TREATMENT OF ASTHMA

'ENGLATE' combines theophylline sodium with glycine, which acts as a powerful buffer against gastric hydrochloric acid and thus reduces the precipitation of theophylline. Theophylline sodium glycinate causes less gastro-intestinal disturbances than other xanthine compounds and can therefore be prescribed in larger doses to obtain maximum theophylline activity.

*'ENGLATE' syrup is specially recommended for children up to 12 years in preference to tablets.*

## ENGLATE

REGD. TRADE MARK

*Brand of theophylline sodium glycinate*

**TABLETS OR SYRUP**

*Samples and literature will gladly be sent on request.*

A NICHOLAS N PRODUCT

A. & G. NICHOLAS LTD. ETHICAL PHARMACEUTICALS, SLOUGH ENGLAND

An M&B brand Medical Product

SULPHATHIAZOLE
SULPHADIAZINE
SULPHAMERAZINE
STREPTOMYCIN

*Introducing*

'STREPTOTRIAD'
trade mark brand
STREPTOMYCIN / TRISULPHONAMIDE

* COMBINED ACTIVITY OF 3 POTENT SULPHONAMIDES WITH STREPTOMYCIN FOR THE TREATMENT OF BACILLARY DYSENTERY
* THE SYSTEMIC ACTION OF THE SULPHONAMIDES HAS A RAPID EFFECT ON THE ACUTE PHASE OF DYSENTERY
* THE UNABSORBED STREPTOMYCIN IS EFFECTIVE IN THE GUT
* LITTLE LIKELIHOOD OF SIDE-EFFECTS BECAUSE MIXED SULPHONAMIDES ARE USED.

'Streptotriad' is presented as pink uncoated tablets each containing streptomycin 65 mg. (in the form of the sulphate), sulphathiazole 100 mg., sulphadiazine 100 mg. and sulphamerazine 65 mg.
Detailed information is available on request

MANUFACTURED BY MAY & BAKER LTD

HA4677

DISTRIBUTORS: PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD · DAGENHAM

# RELIABLE
# ORAL TREATMENT

*for most common infections*

---

# 'DISTAQUAINE' V

The original British Penicillin V

---

Tablets of 60, 120 and 240 mg.

**DOSAGE:** 1 or 2 tablets every four hours

*Also available:*

'DISTAQUAINE' V ELIXIR and 'DISTAQUAINE' V SULPHA tablets

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**THE DISTILLERS COMPANY *(Biochemicals)* LIMITED**

Broadway House, The Broadway, Wimbledon, London S.W.19

TELEPHONE: LIBERTY 6600

PPH 16/57

FOR SOUND SLEEP AND CLEAR AWAKENING

# Doriden

*(α-phenyl-α-glutarimide)*

## A General Purpose

## Non-Barbiturate Hypnotic

RAPID ACTION (20-30 MINUTES)

OF MEDIUM DURATION (4-6 HOURS)

*Tablets containing 0.25g. Doriden are available in bottles of 25, 100 and 500*

CIBA

*'Doriden' is a registered trade mark. Reg. user*

CIBA LABORATORIES LIMITED, HORSHAM, SUSSEX

Telephone: Horsham 4321 Telegrams: Cibalabs, Horsham

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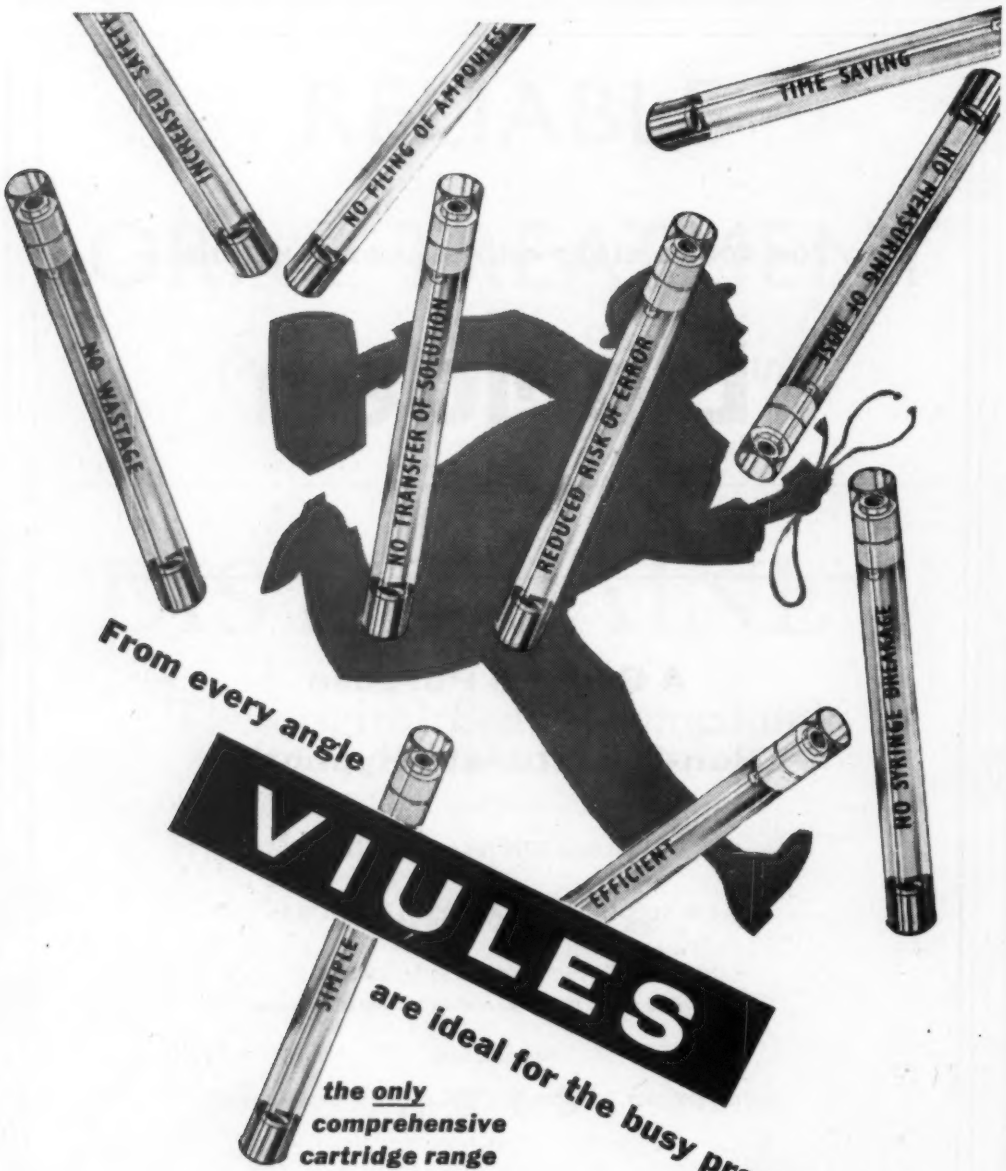


**SAFE • SURE • SIMPLE & SPEEDY**

the Viule injection technique in use throughout the world, offers outstanding advantages at no extra cost. Details of the syringe and a list of the wide range of drugs available will be gladly sent on request.

*Literature and further information gladly sent on request*

**BOOTS PURE DRUG COMPANY LIMITED NOTTINGHAM ENGLAND**

Boots

8303

*The order of the day...*

**'LANOXIN'** *for maintenance therapy*

It never varies in potency.

It is taken each day, not intermittently.

Over-digitalisation quickly subsides because of rapid excretion.

**'LANOXIN'** BRAND *for unfailing control*

**DIGOXIN**

BURROUGHS WELLCOME & CO. *(The Wellcome Foundation Ltd.)* LONDON

# A new approach to the treatment of Rheumatoid Disease

RECENT WORK has shown that chloroquine administered in small daily doses (1-2 tablets 'Avloclor') can produce good to excellent results in the control of rheumatoid disease, particularly rheumatoid arthritis. The treatment is safe and free from serious side effects. Moreover, unlike the steroids, it has the advantage that it can be given over a prolonged period without influencing the adrenal, the pituitary, or any other internal function.

**'Avloclor'** *Chloroquine Phosphate B.P.*

issued in bisected tablets of 0.25 gramme
*(equivalent to 0.15 gramme base)*

*Literature and further information available on request*

IMPERIAL CHEMICAL INDUSTRIES LIMITED Pharmaceuticals Division Wilmslow Cheshire

Ph.786

# PREDICTION OF SERUM-CHOLESTEROL RESPONSES OF MAN TO CHANGES IN FATS IN THE DIET*

ANCEL KEYS
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JOSEPH T. ANDERSON
Ph.D. Rochester
FRANCISCO GRANDE
M.D. Madrid
*From the Laboratory of Physiological Hygiene of the University of Minnesota, Minneapolis, and Hastings State Hospital, Minnesota*

A SHARP decrease in the amount of ordinary fats in the usual American or Western European diet, without any change in the amount of calories or vitamins, lowers the serum-cholesterol level. The fall is rapid in the first few days, but after a few weeks there is an approach to a new plateau (Keys et al. 1950, Mellinkoff et al. 1950, Groen et al. 1952, Keys 1952, Keys et al. 1955). Such low-fat diets usually contain less cholesterol and animal proteins, but the change in the serum-cholesterol level in man does not depend on this fact (Keys et al. 1956b, Keys and Anderson 1957). The responsible agent is clearly either in the quality of the fats or in the ratio of fat to carbohydrate calories.

The most striking difference between an ordinary American diet and a low-fat diet is in the amount of animal fat. The usual diets of 119 Minnesota businessmen were measured with great care in 1953–54 by a team headed by Miss Sadye Adelson from the U.S. Department of Agriculture Research Service; they showed an average intake of 115 g. of fat, of which 85 g. was animal fat. Diets containing very little fat may provide less than 5 g. of animal fat (a decrease of 94%), whereas the vegetable fat in such diets may amount to 15–20 g. (a decrease of 40–50%). A moderately low-fat diet for such men would contain something like 50 g. of total fat, half from animal sources, making a decrease of 5 g. of vegetable fat and 70 g. of animal fat. Such a change in diet quickly lowers the serum-cholesterol level.

It is tempting, then, to ascribe the effect of low-fat diets to the decrease in animal fat, especially since some vegetable oils given in large amounts in synthetic concoctions may depress the serum-cholesterol level (Kinsell et al. 1952, Ahrens et al. 1954, Bronte-Stewart et al. 1956, Beveridge et al. 1956). However, the free use of vegetable fat in otherwise low-fat diets may raise the serum-cholesterol level (Keys et al. 1950). Clearly the analysis of the effects of dietary fats on the serum-cholesterol should be made in terms of chemical composition rather than of origin.

Accordingly for the past six years we have conducted controlled dietary experiments in the metabolic research unit of the Hastings State Hospital, using diets with fixed adequate amounts of calories, proteins, and vitamins but with different amounts and kinds of fats (Anderson et al. 1957). Most of the dietary comparisons were made from both forward and backward dietary changes—i.e., changing from diet X to diet Y and vice versa. Standard periods on each diet were from two to nine weeks, usually four weeks. In all the experiments the experimental diets were preceded by at least four weeks' standardisation on fixed "normal" diets. In each series of experiments 12–27 men were studied on each of two to six diets. In addition we have the data from three experiments in Shime, Japan, on Japanese coalminers (Keys et al. 1957b).

We report here the serum-cholesterol responses to different amounts of dietary glycerides of saturated (S), monoethenoid (M), and polyethenoid (P) fatty acids producing 9–44% of calories derived from fats. Besides normal "house diets" and low-fat diets, the experiments involved commercial grades of butter-fat, olive oil, cotton-seed oil, corn oil, sunflower-seed oil, hydrogenated coconut oil ('Hydrol'), sardine oil, safflower oil, several varieties of margarine, and the mixed fats of ordinary American diets.

## Diets

Our aim was to obtain information about the effects of the fatty acids in the presence of ordinary foods in mixed diets; so formula and synthetic diets were not used. Calorie equilibrium was maintained at all times. The calorie requirements of the individual men at Hastings were estimated by measuring the intakes of food at constant body-weight during a control period of four weeks before each of the series of experiments. In the Shime experiments (Keys et al. 1957b) the change in the diet was an isocaloric substitution of fat (butter-fat or one of two kinds of margarine) for 450 calories of rice carbohydrate, the regular diet of the men otherwise being continued throughout; there was no significant change in body-weight.

The diets in the Hastings experiments conformed to the general pattern of menus in the United States, 37–42% of calories being from fats and 13–15% from proteins, and the day's calories being apportioned roughly as 25%, 35%, and 40% for breakfast, luncheon, and dinner respectively. Seven rotating "house-diet" menus were devised so that the individual calorie requirements were easily supplied by altering the allowances of jam, sugar, potatoes, and bread. Similarly seven menus of "low-fat-base" diet were devised to resemble the house diet except that the fats and the corresponding calories were much decreased, the whole being arranged so that either an experimental fat or carbohydrates (jam, sugar, potatoes, and bread) could be added to bring the total amount of calories to that needed for equilibrium. These house and low-fat-base diets varied slightly from one set of experiments to another, but the nutrient contents are exemplified in table 1 as computed from average values for the nutrients in each of the food items in each day's menu.

The low-fat-base diet provided an average of about 400 mg. less cholesterol daily than did the corresponding house diet, but variations of twice this amount of cholesterol are without effect on the serum-cholesterol level (Keys et al. 1956b). The low-fat-base diet also tended to average 5–10 mg. lower in the daily tocopherol content than did the house diet, but in unpublished experiments we have found that even the addition of 100 mg. of α-tocopherol to the daily diet has no effect on the serum-cholesterol level.

The house and low-fat-base diets at Hastings were closely matched in total proteins, and there was no major difference in the proportions of proteins from animal and vegetable sources in the two kinds of diets. This agreement was assured by the use of casein, egg-white, and skim-milk in the low-fat-base diets. In any case, large differences in the amount of animal protein (±10% of calories in the form of casein) in such diets have no significant influence on the serum-cholesterol level of man (Keys and Anderson 1957).

Measurements of body-weight and of the foods eaten by each man during the preliminary control periods at Hastings were used in estimating the calorie requirements to maintain equilibrium during the experimental periods. These individual allowances were adjusted weekly, if

* The data cited here were obtained with the help of research grants from the National Dairy Council, Chicago; the Minnesota Heart Association; the Nutrition Foundation, New York; the American Heart Association; the Schweppe Foundation, Chicago; the Winton Companies Fund; and Mr. David Winton, of Minneapolis.

TABLE I—NUTRIENT CONTENTS OF REPRESENTATIVE HOUSE AND LOW-FAT-BASE DIETS IN THE HASTINGS EXPERIMENTS

| Diet | Day | Cal. | Prot. (g.) | Total fat (g.) | Vit. A I.U. | Aneurine (mg.) | Riboflavine (mg.) | Nicotinic acid (mg.) | Pyridoxine (mg.) | Ascorbic acid (mg.) | Tocopherol (mg.) | Phytosterol (mg.) | Cholesterol (mg.) | Iron (mg.) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| House | 1 | 3159 | 101 | 138 | 4600 | 2·1 | 2·4 | 23 | 1·9 | 71 | 56 | 91 | 1110 | 15 |
| ,, | 2 | 3217 | 98 | 136 | 10,600 | 1·8 | 2·2 | 20 | 2·4 | 158 | 9 | 57 | 680 | 16 |
| ,, | 3 | 3183 | 98 | 139 | 5000 | 3·3 | 2·1 | 13 | 1·1 | 68 | 8 | 75 | 730 | 13 |
| ,, | 4 | 3173 | 102 | 140 | 3300 | 2·7 | 2·4 | 20 | 1·3 | 136 | 7 | 64 | 510 | 16 |
| ,, | 5 | 3208 | 99 | 138 | 17,100 | 1·6 | 2·4 | 17 | 1·8 | 71 | 8 | 60 | 870 | 16 |
| ,, | 6 | 3219 | 94 | 136 | 22,800 | 1·3 | 2·2 | 19 | 1·8 | 97 | 11 | 94 | 690 | 20 |
| ,, | 7 | 3195 | 103 | 137 | 8100 | 1·7 | 2·1 | 23 | 2·5 | 128 | 7 | 80 | 610 | 17 |
| ,, | Mean | 3183 | 99 | 138 | 10,200 | 2·1 | 2·2 | 19 | 1·8 | 104 | 15 | 74 | 740 | 16 |
| Low-fat-base | 1 | 2290 | 99 | 39 | 17,900 | 1·8 | 3·0 | 18 | 1·8 | 128 | 6 | 49 | 340 | 18 |
| ,, | 2 | 2290 | 99 | 38 | 8800 | 1·3 | 2·9 | 23 | 1·8 | 162 | 7 | 70 | 280 | 21 |
| ,, | 3 | 2330 | 101 | 39 | 17,100 | 1·8 | 2·9 | 19 | 1·7 | 84 | 8 | 83 | 280 | 17 |
| ,, | 4 | 2290 | 97 | 37 | 3400 | 1·7 | 2·8 | 17 | 1·8 | 100 | 4 | 41 | 280 | 17 |
| ,, | 5 | 2320 | 102 | 37 | 2000 | 1·8 | 3·1 | 20 | 2·1 | 101 | 5 | 75 | 300 | 16 |
| ,, | 6 | 2340 | 100 | 40 | 3700 | 1·7 | 2·9 | 19 | 1·9 | 148 | 5 | 59 | 310 | 16 |
| ,, | 7 | 2320 | 102 | 41 | 3600 | 1·6 | 2·8 | 18 | 2·1 | 105 | 5 | 66 | 300 | 19 |
| ,, | Mean | 2311 | 100 | 39 | 8100 | 1·8 | 2·9 | 19 | 1·9 | 118 | 6 | 63 | 300 | 18 |
| Experimental fat | .. | 900 | .. | 100 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| ,, ,, + L.F.B. | .. | 3211 | .. | 139 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |

needed, during the experimental periods according to the indications from the weekly (nude) body-weights. These calorie adjustments were made by changing the allowances of sugar, jam, potatoes, and bread. A change of 3 kg. or more in body-weight over an entire experiment was considered to indicate failure to maintain calorie equilibrium.

At Hastings the men were under surveillance by special attendants for 24 hours daily both in the quarters where they spent most of the time and during their standardised outdoor recreation. Fixed recipes were followed, all food servings were measured, and plate waste and extra portions were recorded for each man. All experimental fats were purchased in large lots and stored in full sealed containers at −20°C until used. Other staple foods were similarly bought in large lots and stored. Bread was baked on the premises. Fresh milk and eggs were procured from a constant local source. The meals were prepared and served in a special diet kitchen, used for no other purpose, within the metabolic research unit. In the Shime series the butter and margarines used were single lots, of which sealed samples were sent by air to the United States for analysis.

### Analytical Methods

Serum-cholesterol was determined in duplicate on samples of venous blood drawn with the patient at rest, in most cases on two occasions, a day or two apart, at the end of each dietary period. These samples were analysed in duplicate, and the average of the four results was taken to be the best estimate of the true value. The method was that of Abell et al. (1952) modified by Anderson and Keys (1956). β-lipoprotein cholesterol was also measured in most of the experiments by the method of Anderson and Keys (1956) but the results are not reported here.

TABLE II—ANALYTICAL VALUES OBTAINED ON FATS USED IN DIETARY EXPERIMENTS

| Fat | Iodine value | Glycerides of fatty acids (%) | | |
|---|---|---|---|---|
| | | Saturated | Monoethenoid | Polyethenoid |
| Butterfat 1 | 32 | 57 | 39 | 4 |
| ,, 2 | 35 | 56 | 39 | 5 |
| Coconut oil (hydrol) | 3 | 97 | 3 | 0 |
| Corn oil 1 | 120 | 12 | 37 | 51 |
| ,, ,, 2 | 128 | 16 | 26 | 58 |
| Cotton-seed oil | 108 | 25 | 25 | 50 |
| Olive oil 1 | 85 | 12 | 80 | 8 |
| ,, ,, 2 | 86 | 13 | 75 | 12 |
| ,, ,, 3 | 85 | 15 | 72 | 12 |
| Margarine A | 39 | 65 | 25 | 10 |
| ,, B (all veg.) | 37 | 64 | 30 | 6 |
| Safflower oil 1 | 144 | 12 | 10 | 78 |
| ,, ,, 2 | 144 | 14 | 8 | 78 |
| ,, ,, 3 | 146 | 10 | 12 | 78 |
| Sardine oil * | 188 | 23 | 23 | 54 |
| Sunflower-seed oil | 131 | 10 | 28 | 62 |

* Fatty acid composition from Brocklesby and Harding (1938) and Hilditch (1956) for *Sardinops cærulea* oil of same iodine value.

The fat analyses were made by the methods recommended by the American Oil Chemists' Society (1950). For the experimental fats and oils values were obtained for unconjugated dienes, trienes, tetraenes, monoenes, saturated fatty acids, conjugated dienes, non-saponifiable lipid, and the percentage of trans acids. Such detailed analysis of the "sardine" oil (from *Sardinops cærulea*) was not attempted, but the iodine and saponification values of the oil used agreed well with samples of the same oil analysed in detail by Brocklesby and Harding (1938).

### Subjects

The men at Hastings were "stabilised" schizophrenics judged, on the basis of extensive examinations and tests, to be physically and metabolically normal.† Men who became ill or otherwise deviated, as well as those whose body-weight changed as much as 3 kg. in an experiment, were excluded. 66 men served successfully as subjects. They were aged 32–56, except 1 man in one experiment who was aged 62. None of them was unusually thin or fat, but on the average they were about 10% lighter in weight than the average of Minnesota businessmen of the same age and height (Anderson et al. 1957). Their average height was 173·5 cm. (5 ft. 8 in.) and average weight (nude) 69·8 kg. (10 st. 13½ lb.).

At Shime the subjects were 18 Japanese men, aged 22–54 (average 39·8), working at their regular occupations as coalminers (Keys et al. 1957b). All were judged clinically healthy on the basis of physical examinations and blood analyses. None was unusually thin or fat. Initially there were 21 Japanese, but 3 were discarded: 1 developed a cold with fever, 1 developed persistent diarrhœa ascribed to the unaccustomed fat in the diet, and 1 lost 2 kg. of weight.

### Fatty-acid Composition of Experimental Fats

The iodine and saponification values of the experimental fats and oils were measured in this laboratory, and estimates of fatty-acid composition were obtained from Bailey (1951), Eckey (1954), and Hilditch (1956) for

† Permission for each subject to participate in these trials was obtained in writing from his nearest relative. The trials were conducted under careful and continuous medical supervision, and the patients were at all times friendly and cooperative.

samples of the same fats having iodine values matching the samples used here. These values were used in devising the diets.

Detailed analyses of the fats were made on samples of fats and oils sent to the Research and Development Department, Miami Valley (Ohio) Laboratories of the Procter and Gamble Co.; Dr. J. C. Cowan at the Northern Utilisation Research Branch (Peoria, Illinois) of the Agricultural Research Service, U.S. Department of Agriculture; and Dr. Raymond Paschke, Research Laboratories of General Mills, Inc. (Minneapolis). Dr. Ralph Holman, of the Hormel Research Institute, Austin, Minnesota, measured the percentages of polyethenoids independently in four kinds of fats.

Table II summarises the analyses of the experimental fats and oils expressed as percentages of the glycerides in the form of saturated (S), monoethenoid (M), and polyethenoid (P) fatty acids. The last-named grouping was adopted because of uncertainties of analysis and identification within the polyethenoids and because, as will appear later, a more elaborate classification of the polyethenoids seems to be unnecessary for the present purpose. These analytical results are in good agreement with those previously published for the same fats and oils with similar iodine values. Trans acids were negligible except in the margarines.

### Fatty-acid Composition of Diets

From data published by Bailey (1951), Eckey (1954), and Hilditch (1956) and from a few special analyses of foods used here a table was compiled for the average fatty-acid composition (S, M, and P) of about 96% of the fats in the foods used in the Hastings and Minneapolis experiments.

The remaining 4% of the dietary fat was in low-fat vegetables and fruits for which it was impracticable to estimate fatty acids for every item separately. The average for this latter group of items was estimated to be 10% saturated, 30% monoethenoid, and 60% polyethenoid fatty acids, and these figures were applied in the computations. Since only 4% of the total fat was involved, at worst no more than trivial errors could result.

In most of the diets used at Hastings the comparisons were between the effects of different test fats added to a constant low-fat-base diet; hence the only variable was the 70–75% of the total dietary fat represented by the experimental fat for which detailed analyses were available.

TABLE III—COMPARISON OF ESTIMATED AND ANALYSED PERCENTAGES OF FATTY-ACID GLYCERIDES OF SATURATED MONOETHENOID, AND POLYETHENOID FATTY ACIDS IN DIETS USED AT HASTINGS

| No. | Diet code | Fat (g. daily) | Diet type | Source of data | Fat (%) | | |
|---|---|---|---|---|---|---|---|
| | | | | | S | M | P |
| 1 | 1KH | 138·2 | House, as served | Estimate | 47·2 | 45·1 | 7·7 |
| | ,, | ,, | ,, ,, ,, | Analysis | 53·3 | 39·4 | 7·3 |
| 2 | 4KH | 137·4 | House, as served | Estimate | 48·6 | 44·6 | 6·8 |
| | ,, | ,, | ,, ,, ,, | Analysis | 47·5 | 45·3 | 7·2 |
| 3 | 2MB | 38·3 | Low fat base M | Estimate | 46·0 | 43·3 | 10·7 |
| | ,, | ,, | ,, ,, ,, ,, | Analysis | 43·3 | 46·2 | 10·5 |
| 4 | 2M18C | 138·3 | M18C as served | Estimate | 51·5 | 43·1 | 5·4 |
| | ,, | ,, | ,, ,, ,, | Analysis | 50·8 | 43·9 | 5·3 |
| 5 | 2M12C | 138·3 | M12C as served | Estimate | 52·1 | 42·7 | 5·2 |
| | ,, | ,, | ,, ,, ,, | Analysis | 51·3 | 43·4 | 5·3 |
| 6 | 3N | 37·8 | Low fat base N | Estimate | 46·0 | 43·1 | 10·9 |
| | ,, | ,, | ,, ,, ,, ,, | Analysis | 42·1 | 49·5 | 8·4 |
| 7 | 3NCr | 137·8 | NCr as served | Estimate | 21·6 | 31·5 | 46·9 |
| | ,, | ,, | ,, ,, ,, | Analysis | 20·6 | 33·2 | 46·2 |
| 8 | 3NSa | 137·8 | NSa as served | Estimate | 21·3 | 19·9 | 58·8 |
| | ,, | ,, | ,, ,, ,, | Analysis | 20·2 | 20·8 | 59·0 |

Pure estimates versus direct analysis are shown for items 1, 2, 3 and 6. For items 4, 5, 7, and 8 analytical data on experimental fats were used in both "Estimate" and "Analysis" values for diets as served.

TABLE IV—INTRA-INDIVIDUAL VARIABILITY OF SERUM-CHOLESTEROL LEVEL (MG. PER 100 ML.) INDICATED BY VALUES OBTAINED 1 OR 2 WEEKS APART IN MEN SUBSISTING IN CALORIE EQUILIBRIUM ON RIGIDLY CONTROLLED DIET

| — | — | Hastings men | U.S. army soldiers |
|---|---|---|---|
| 1 | N .. .. .. .. .. | 834 | 38 |
| 2 | $\Sigma\Delta^2/2N = (S.E.M.)^2$ .. | 132 | 144 |
| 3 | S.E.M. .. .. .. | ±11·52 | ±12·00 |
| 4 | S.E. of S.E.M. .. .. | ±0·28 | ±1·38 |
| 5 | Grand mean cholesterol | 228·2 | 209·7 |
| 6 | 100 × line 3/line 5 .. | ±5·04% | ±5·72% |

Direct analyses were made of the entire combined foods of representative weeks of house and low-fat-base diets. The procedure was to set a dummy place at each meal for a week and to serve this dummy the specified amounts of each item in the menu for that day. Each meal was mixed and ground immediately after the food items had been measured out, and the mixture was stored at −20°C until the week's collection was completed. At the end of the week the entire collection of twenty-one meals was thawed, mixed, and passed through a meat-grinder, a measured amount of water being added to facilitate mixing. Checks of beginning and end weights showed an average of 99·5% of food weight accounted for. Weighed portions of this diluted mixture were mixed in a Waring blender. Portions of this final slurry were frozen on the walls of wide-mouthed short flasks and dried in vacuo from the frozen state. The dried residue was saponified, acidified, and extracted with ethyl ether. After evaporation of the solvent in vacuo the lipid was dissolved in petroleum ether and kept at −20° until analysed.

Table III gives the analytical results obtained in this way from two weeks of house diets and from two weeks of low-fat-base diets, together with the corresponding composition computed by adding the estimated average values for each of the foodstuffs. Table III also shows the analyses of four experimental fat diets as served and, for comparison, the corresponding values obtained by adding the known values for the (analysed) test fats to the estimates for the low-fat-base diets.

The estimated and analytical values agree very well, particularly for the polyethenoids (P in table III). For the low-fat-base diets plus added test fats—i.e., experimental diets as actually served (items 4, 5, 7, 8 in table III)—no discrepancy larger than 1% was observed. With the house diets the estimates tended to be slightly too low for saturated fats (average −2·2%) and slightly too high for monoethenoids (average +2·5%); these differences approach the limits of analytical and sampling error for fatty acids in such mixed fats.

### Variability in Serum-cholesterol Levels

Consideration of the reliability of estimates of serum-cholesterol levels and of intra- and inter-individual variability is essential for analysing the results of dietary experiments. For this purpose we have 3336 cholesterol analyses comprising 834 sets of measurements on 66 men at Hastings, each set consisting of analyses in duplicate on each of two samples of blood drawn one or two weeks apart from 1 man subsisting on a controlled fixed diet maintained for at least three weeks before drawing the first sample. Table IV summarises this material. The standard error of measurement (S.E.M.) in the 1668 pairs of duplicate analyses in this series is ±3·64 mg. of cholesterol per 100 ml. of serum, calculated from the sum of the differences between duplicates ($\Delta$), without regard to sign, as $(S.E.M.)^2 = \Sigma\Delta^2/2N$. This is a measure of analytical error. The variability of the men is indicated by calculating the S.E.M. in the same way

TABLE V—SERUM-CHOLESTEROL LEVELS * AT HASTINGS ON HOUSE DIET ON TWO OCCASIONS 1 WEEK APART AND CHANGES DURING SUCCESSIVE WEEKS ON LOW-FAT DIET

| Case no. | House diet | | Δ on low-fat diet for weeks | | | | |
|---|---|---|---|---|---|---|---|
| | 31 Jan. | 7 Feb. | 1 | 2 | 3, 4 | 5, 6 | 7, 8, 9 |
| 1 | 206 | 209 | −15 | −33 | −28 | −37 | −24 |
| 2 | 224 | 236 | − 9 | −22 | − 6 | + 3 | −52 |
| 3 | 174 | 167 | −23 | −23 | −36 | −33 | −25 |
| 4 | 160 | 184 | −26 | −17 | −19 | − 7 | −22 |
| 5 | 184 | 196 | −30 | −22 | −17 | −30 | −33 |
| 6 | 301 | 291 | −29 | −63 | −63 | −66 | −50 |
| 7 | 240 | 238 | −50 | −75 | −66 | −61 | −36 |
| 8 | 281 | 264 | −49 | −74 | −73 | −87 | −94 |
| 9 | 228 | 240 | −22 | −54 | −28 | −39 | −39 |
| 10 | 172 | 166 | −13 | −33 | −16 | −26 | −24 |
| 11 | 227 | 236 | −39 | −38 | −31 | −37 | −33 |
| 12 | 201 | 173 | + 1 | + 2 | − 4 | + 6 | −15 |
| 13 | 284 | 251 | −24 | −42 | −52 | −51 | −37 |
| 14 | 240 | 230 | −17 | −25 | +11 | − 8 | −18 |
| Mean | 223·0 | 220·1 | −24·6 | −37·1 | −30·6 | −33·8 | −35·9 |
| S.E. | ±11·7 | ±10·3 | ± 3·8 | ± 6·0 | ± 6·7 | ± 7·2 | ± 5·3 |

* Mg. per 100 ml.

but using for Δ the difference between the means of the values recorded for the first and second occasions; this gave S.E.M. = ±11·52 mg. per 100 ml., or ±5·04% of the grand mean cholesterol level.

For comparison we have data from 38 American soldiers maintained in the laboratory for a month on a constant ration with rigidly standardised conditions of exercise and rest. The intra-individual variability does not significantly differ from that of the men at Hastings.

The variability between individuals is still greater, of course, even when we are concerned only with clinically healthy men of the same age, engaged in the same activity, and eating precisely the same diet. The inter-individual variability in the Hastings experiments is indicated by the standard deviations of the mean values at the ends of the experimental periods, these means being computed from the averages for each man, for whom two samples were analysed, each in duplicate. The grand average of these standard deviations was ±33·58 mg. per 100 ml., or ±14·7% of the grand mean serum-cholesterol level.

Table v illustrates the intra- and inter-individual variability as well as the variability in the serum-cholesterol response to a change in dietary fat. This experiment was selected for illustration because the variability is about as large as is ever encountered in these experiments, and because the experiment lasted long enough to show the characteristic time course of the response. A highly significant change in the serum-cholesterol level takes place within a week after a change in diet fat; by the end of the second week a relative plateau is reached, and no further significant change can be observed within the next month or two.

### Experimental Data and their Analysis

The experimental data are summarised in table vi. The fats in the diets are expressed as percentages of the total calories contributed by glycerides of saturated (S), monoethenoid (M), and polyethenoid (P) fatty acids. Table vi gives the means (and standard errors) of serum-cholesterol levels for the groups of men at the end of each dietary period. The problem then is to discover whether the differences between the serum-cholesterol levels on these diets are systematically related to these dietary variables, and how such a relationship is best expressed.

For a given group of men the average serum-cholesterol level in calorie equilibrium on a given diet may be related to the diet composition:

$$(1) \qquad \text{Chol.}_1 = a + b\text{S}_1 + c\text{M}_1 + d\text{P}_1$$

where Chol. is the serum-cholesterol level in mg. per 100 ml., $a$ is a characteristic of the particular group of men, independent of the diet fat, and $b$, $c$, and $d$ are multiplying coefficients that express the influence of S, M, and P respectively per unit of those dietary factors. On a different diet, everything else being the same, it would follow that:

$$\text{Chol.}_2 = a + b\text{S}_2 + c\text{M}_2 + d\text{P}_2;$$

so the change in the serum-cholesterol level is indicated by subtraction:

$$(2) \qquad \Delta\,\text{Chol.}_{1,2} = b(\text{S}_1 - \text{S}_2) + c(\text{M}_1 - \text{M}_2) + d(\text{P}_1 - \text{P}_2).$$

Table vii gives the 64 sets of such differences available for the solution of equation 2. For the initial analysis the data marked with asterisks were omitted because (1) the effects of corn oil may not be fully explained in terms of fatty-acid composition (Keys et al. 1957a); (2) the polyethenoids in fish oils may not be comparable with those in other foods; (3) the men in Japan may not be comparable with the men in Minnesota; and (4) preliminary analysis has suggested that hydrol may require special consideration.

There were, then, 41 sets of comparisons available for the initial analysis, 10 being in a single series, JWX. Least-squares solutions of equation 2 were obtained by the method of matrices for these JWX data and, separately, for the 31 other sets of data. Statistical tests showed that the regressions and the component variances

TABLE VI—AVERAGE PERCENTAGES OF TOTAL CALORIES FROM GLYCERIDES OF S, M, AND P FATTY ACIDS FOR EACH DIETARY PERIOD AND MEAN (AND STANDARD ERROR) TOTAL SERUM-CHOLESTEROL LEVELS AT END OF EACH DIETARY PERIOD

| Expt. no. | Diet type | No. of men | Calories from fats (%) | | | | Serum-chol. (mg. per 100 ml.) |
|---|---|---|---|---|---|---|---|
| | | | Total | S | M | P | |
| C | Low-fat | 16 | 8·5 | 3·7 | 3·5 | 1·3 | 198·2 ± 7·0 |
| ,, | Olive oil | ,, | 25·2 | 5·6 | 17·4 | 2·2 | 213·6 ± 9·1 |
| ,, | Cotton-seed oil | ,, | 25·1 | 7·8 | 7·7 | 9·4 | 208·8 ± 10·2 |
| D | House | 12 | 37·7 | 17·2 | 17·1 | 3·4 | 225·2 ± 10·7 |
| ,, | Low-fat | ,, | 15·9 | 7·0 | 7·2 | 1·7 | 198·1 ± 9·1 |
| ,, | Butter-fat | ,, | 39·5 | 18·3 | 15·2 | 6·0 | 231·9 ± 9·2 |
| ,, | Cotton-seed oil + marg. | ,, | 38·4 | 14·9 | 16·5 | 7·0 | 211·9 ± 9·4 |
| F | House | 18 | 40·0 | 18·8 | 17·8 | 3·4 | 231·8 ± 11·1 |
| ,, | Butter-fat | ,, | 37·8 | 20·4 | 15·0 | 2·4 | 234·8 ± 8·5 |
| ,, | Low-fat | ,, | 11·4 | 5·2 | 4·8 | 1·4 | 203·0 ± 7·9 |
| ,, | Cotton-seed oil | ,, | 37·7 | 11·9 | 11·2 | 14·6 | 203·4 ± 11·3 |
| G | House | 27 | 36·7 | 16·4 | 16·2 | 4·1 | 222·3 ± 7·3 |
| ,, | Lard | ,, | 37·8 | 15·7 | 18·0 | 4·1 | 221·4 ± 9·5 |
| ,, | Butter-fat | ,, | 37·8 | 20·6 | 14·5 | 2·7 | 240·9 ± 8·0 |
| HWX | House | 13 | 40·8 | 18·7 | 19·4 | 2·7 | 221·3 ± 11·7 |
| ,, | Low-fat | ,, | 11·4 | 4·7 | 5·2 | 1·5 | 186·3 ± 9·3 |
| ,, | Cotton-seed oil | ,, | 37·0 | 10·9 | 11·3 | 14·8 | 179·5 ± 10·1 |
| ,, | Corn oil | ,, | 37·4 | 7·5 | 13·6 | 16·3 | 160·2 ± 9·0 |
| HYZ | House | 12 | 41·1 | 18·9 | 19·2 | 3·0 | 213·3 ± 8·2 |
| ,, | Low-fat | ,, | 11·8 | 4·8 | 5·4 | 1·6 | 181·0 ± 7·2 |
| ,, | Cotton-seed oil | ,, | 37·5 | 11·1 | 11·6 | 14·8 | 178·2 ± 8·8 |
| JWX | House | 14 | 40·8 | 18·7 | 19·2 | 2·9 | 219·9 ± 11·0 |
| ,, | Butter-fat | ,, | 36·8 | 19·3 | 15·6 | 1·9 | 223·5 ± 9·1 |
| ,, | Low-fat | ,, | 11·3 | 5·1 | 5·4 | 0·8 | 184·7 ± 5·8 |
| ,, | Olive oil | ,, | 37·4 | 7·9 | 26·7 | 2·8 | 187·9 ± 8·4 |
| ,, | Sunflower-seed oil | ,, | 37·0 | 7·4 | 12·7 | 16·9 | 170·0 ± 9·0 |
| ,, | Corn oil | ,, | 37·6 | 7·6 | 14·6 | 15·4 | 160·7 ± 9·2 |
| JYZ | House | 12 | 41·9 | 19·6 | 19·7 | 2·9 | 220·1 ± 10·1 |
| ,, | Butter-fat | ,, | 38·8 | 21·0 | 16·0 | 1·8 | 219·2 ± 9·4 |
| ,, | Cotton-seed oil | ,, | 39·2 | 12·0 | 12·0 | 15·2 | 183·7 ± 7·3 |
| ,, | Olive oil | ,, | 39·3 | 8·1 | 28·3 | 2·9 | 189·9 ± 6·6 |
| ,, | Sardine oil | ,, | 39·2 | 11·4 | 11·9 | 15·9 | 179·8 ± 5·2 |
| ,, | Corn oil | ,, | 39·0 | 7·8 | 14·6 | 16·6 | 159·7 ± 9·0 |
| KWY | House | 13 | 36·6 | 17·9 | 16·6 | 2·1 | 206·1 ± 6·9 |
| ,, | Safflower oil | ,, | 44·4 | 18·9 | 17·3 | 8·2 | 196·5 ± 6·8 |
| Shime (A) | Control | 7 | 10·3 | 2·3 | 4·0 | 4·0 | 145·4 ± 14·4 |
| ,, | Butter-fat | ,, | 22·6 | 9·7 | 8·4 | 4·5 | 163·0 |
| (B) | Control | 6 | 10·3 | 2·3 | 4·0 | 4·0 | 135·7 ± 11·0 |
| ,, | Margarine 1 | ,, | 22·6 | 10·3 | 7·1 | 5·2 | 154·7 |
| (C) | Control | 5 | 10·3 | 2·3 | 4·0 | 4·0 | 163·2 ± 16·6 |
| ,, | Margarine 2 | ,, | 22·6 | 10·1 | 7·7 | 4·8 | 177·4 |
| HYZ | Hydrol | 12 | 37·6 | 30·6 | 5·9 | 0·9 | 224·3 ± 8·4 |
| ,, | ,, | ,, | ,, | 23·8* | 5·9 | 0·9 | ,, ,, |

* Only fatty acids with 12 or more carbons in the chain counted.

were not significantly different; so it was concluded that pooling of the entire 41 sets of data would be legitimate, and the following solution was obtained for the combined data:

(2a) $\Delta$ Chol. $= -1{\cdot}68 + 2{\cdot}76\Delta S + 0{\cdot}05\Delta M - 1{\cdot}35\Delta P$,

where $\Delta$ Chol. is in mg. per 100 ml.

On testing the significance of the contributions of the several coefficients it is found that, expressing these as t values, we have for $a$, t = 0·98; for $b$, t = 15·15; for $c$, t = 0·36; and for $d$, t = 7·19. Since we have 37 degrees of freedom (41–3–1), both $b$ and $d$ make very highly significant contributions to the prediction, but neither $a$ nor $c$ is significant. Accordingly, the third-order equation (2) may be replaced by a second-order equation; and, further, since the constant $a$ is insignificant, we may stipulate that the final regression equation should pass through the zero-zero origin. New least-squares solutions were then obtained for the equation:

(3) $\Delta$ Chol. $= b\Delta S + d\Delta P$,

for the JWX series, the remaining 8 series, and, since the regressions and variances indicate homogeneity, the combined 41 sets of data. The results of these calculations are given in table VIII.

The final result is:

(3a) $\Delta$ Chol. $= 2{\cdot}74\Delta S - 1{\cdot}31\Delta P$.

The application of equation 3a to these 41 sets of data yields the results shown in the accompanying figure.

TABLE VII—MEAN DIFFERENCES IN PERCENTAGES OF CALORIES IN DIETS PROVIDED BY GLYCERIDES OF (S), (M), AND (P) FATTY ACIDS, TOGETHER WITH CORRESPONDING MEAN (± STANDARD ERROR) DIFFERENCES IN SERUM-CHOLESTEROL AT ENDS OF DIETARY PERIODS

| Expt. no. | Diet comparison | | | Δ Diet fats, % cal. | | | Δ Chol. (mg. per 100 ml.) | |
|---|---|---|---|---|---|---|---|---|
| | | | | S | M | P | Mean | S.E. of mean |
| C | Low-fat | *minus* | olive oil | − 1·9 | −13·9 | − 0·9 | −15·4 | ± 5·8 |
| ,, | ,, | ,, | cotton-seed oil | − 4·1 | − 4·2 | − 8·1 | −10·6 | ± 6·4 |
| ,, | Olive oil | ,, | ,, ,, | − 2·2 | 9·7 | − 7·2 | 4·8 | ± 5·3 |
| D | House | *minus* | low-fat | 10·2 | 9·9 | 1·7 | 27·1 | ± 4·2 |
| ,, | ,, | ,, | butter-fat | − 1·1 | 1·9 | − 2·6 | − 6·7 | ± 4·7 |
| ,, | ,, | ,, | cotton. + marg. | 2·3 | 0·6 | − 3·6 | 13·3 | ± 4·4 |
| ,, | Low-fat | ,, | butter-fat | −11·3 | − 8·0 | − 4·3 | −33·8 | ± 3·7 |
| ,, | ,, | ,, | cotton. + marg. | − 7·9 | − 9·3 | − 5·3 | −13·8 | ± 5·3 |
| ,, | Butter-fat | ,, | ,, ,, | 3·4 | − 1·3 | − 1·0 | 20·0 | ± 5·1 |
| F | House | *minus* | butter-fat | − 1·6 | 2·8 | 1·0 | −12·4 | ± 4·7 |
| ,, | ,, | ,, | low-fat | 13·6 | 13·0 | 2·0 | 28·8 | ± 4·8 |
| ,, | ,, | ,, | cotton-seed oil | 6·9 | 6·6 | −11·2 | 28·4 | ± 3·7 |
| ,, | Butter-fat | ,, | low-fat | 15·2 | 10·2 | 1·0 | 42·4 | ± 4·2 |
| ,, | ,, | ,, | cotton-seed oil | 8·5 | 3·8 | −12·2 | 42·0 | ± 4·9 |
| ,, | Low-fat | ,, | ,, ,, | − 6·7 | − 6·4 | −13·2 | − 0·4 | ± 4·2 |
| G | House | *minus* | lard | 0·7 | − 1·8 | 0·0 | 0·9 | ± 3·3 |
| ,, | ,, | ,, | butter-fat | − 4·2 | 1·7 | 1·4 | −18·6 | ± 3·6 |
| ,, | Lard | ,, | ,, | − 4·9 | 3·5 | 1·4 | −19·5 | ± 3·9 |
| HWX | House | *minus* | low-fat | 14·0 | 14·2 | 1·2 | 35·0 | ± 5·1 |
| ,, | ,, | ,, | cotton-seed oil | 7·8 | 8·1 | −12·1 | 41·8 | ± 4·7 |
| ,, | ,, | ,, | corn oil * | 11·2 | 5·8 | −13·6 | 61·1 | ± 5·4 |
| ,, | Low-fat | ,, | cotton-seed oil | − 6·2 | − 6·1 | −13·3 | − 6·8 | ± 4·4 |
| ,, | ,, | ,, | corn oil * | − 2·8 | − 8·4 | −14·8 | 26·1 | ± 3·9 |
| ,, | Cotton-seed oil | ,, | ,, ,, * | 3·4 | − 2·3 | − 1·5 | 19·3 | ± 4·2 |
| HYZ | House | *minus* | low-fat | 14·1 | 13·8 | 1·4 | 32·3 | ± 5·2 |
| ,, | ,, | ,, | cotton-seed oil | 7·8 | 7·6 | −11·8 | 35·1 | ± 5·0 |
| ,, | ,, | ,, | hydrol * | −11·7 | 13·1 | 1·8 | −11·0 | ± 2·8 |
| ,, | Low-fat | ,, | cotton-seed oil | − 6·3 | − 6·2 | −13·2 | 2·8 | ± 4·5 |
| ,, | ,, | ,, | hydrol * | −25·8 | − 0·7 | 0·4 | −43·3 | ± 7·4 |
| ,, | Cotton-seed oil | ,, | ,, * | −19·5 | 5·5 | 13·6 | −46·1 | ± 6·8 |
| JWX | House | *minus* | butter-fat | − 0·6 | 3·6 | 1·0 | − 3·6 | ± 3·8 |
| ,, | ,, | ,, | low-fat | 13·6 | 13·8 | 2·1 | 35·2 | ± 6·0 |
| ,, | ,, | ,, | olive oil | 10·8 | − 7·5 | 0·1 | 32·0 | ± 6·2 |
| ,, | ,, | ,, | sunflower-seed oil | 11·3 | 6·5 | −14·0 | 49·2 | ± 6·1 |
| ,, | ,, | ,, | corn oil * | 11·1 | 4·6 | −12·5 | 59·2 | ± 5·0 |
| ,, | Butter-fat | ,, | low-fat | 14·2 | 10·2 | 1·1 | 38·8 | ± 6·1 |
| ,, | ,, | ,, | olive oil | 11·4 | −11·1 | − 0·9 | 35·6 | ± 4·7 |
| ,, | ,, | ,, | sunflower-seed oil | 11·9 | 2·9 | −15·0 | 53·5 | ± 7·4 |
| ,, | ,, | ,, | corn oil * | 11·7 | 1·0 | −13·5 | 62·8 | ± 3·5 |
| ,, | Low-fat | ,, | olive oil | − 2·8 | −21·3 | − 2·0 | − 3·2 | ± 5·4 |
| ,, | ,, | ,, | sunflower-seed oil | − 2·3 | − 7·3 | −16·1 | 14·7 | ± 6·3 |
| ,, | ,, | ,, | corn oil * | − 2·5 | − 9·2 | −14·6 | 24·0 | ± 6·1 |
| ,, | Olive oil | *minus* | sunflower-seed oil | 0·5 | 14·0 | −14·1 | 17·9 | ± 5·1 |
| ,, | ,, | ,, | corn oil * | 0·3 | 12·1 | −12·6 | 27·2 | ± 3·6 |
| ,, | Sunflower-seed oil | ,, | ,, ,, * | − 0·2 | − 1·9 | 1·5 | 9·3 | ± 2·8 |
| JYZ | House | *minus* | butter-fat | − 1·4 | 3·7 | 1·1 | 0·9 | ± 4·4 |
| ,, | ,, | ,, | cotton-seed oil | 7·6 | 7·7 | −12·3 | 36·4 | ± 5·1 |
| ,, | ,, | ,, | olive oil | 11·5 | − 8·6 | 0·0 | 30·2 | ± 4·6 |
| ,, | ,, | ,, | sardine oil * | 8·2 | 7·8 | −13·0 | 40·3 | ± 5·3 |
| ,, | ,, | ,, | corn oil * | 11·8 | 5·1 | −13·7 | 60·4 | ± 5·6 |
| ,, | Butter-fat | ,, | cotton-seed oil | 9·0 | 4·0 | −13·4 | 35·5 | ± 5·4 |
| ,, | ,, | ,, | olive oil | 12·9 | −12·3 | − 1·1 | 29·3 | ± 4·3 |
| ,, | ,, | ,, | sardine oil * | 9·6 | 4·1 | −14·1 | 39·4 | ± 5·6 |
| ,, | ,, | ,, | corn oil * | 13·2 | 1·4 | −14·8 | 59·5 | ± 5·7 |
| ,, | Cotton-seed oil | ,, | olive oil | 3·9 | −16·3 | 12·3 | − 6·2 | ± 5·2 |
| ,, | ,, ,, | ,, | sardine oil * | 0·6 | 0·1 | − 0·7 | 3·9 | ± 5·2 |
| ,, | ,, ,, | ,, | corn oil * | 4·2 | − 2·6 | − 1·4 | 24·0 | ± 5·6 |
| ,, | Olive oil | ,, | sardine oil * | − 3·3 | 16·4 | −13·0 | 10·1 | ± 4·6 |
| ,, | ,, ,, | ,, | corn oil * | 0·3 | 13·7 | −13·7 | 30·2 | ± 4·8 |
| ,, | Sardine oil | ,, | ,, ,, * | 3·6 | − 2·7 | − 0·7 | 20·1 | ± 3·8 |
| KWY | House | *minus* | safflower oil | − 1·0 | − 0·7 | − 5·9 | 9·6 | ± 4·4 |
| Shime | | | | | | | | |
| (A) | Control | *minus* | butter-fat * | − 7·4 | − 4·4 | − 0·5 | −17·6 | ± 5·2 |
| (B) | ,, | ,, | margarine 1 * | − 8·0 | − 3·1 | − 1·2 | −19·0 | ± 8·0 |
| (C) | ,, | ,, | ,, 2 * | − 7·8 | − 3·7 | − 0·8 | −14·2 | ± 6·9 |

* See text.

TABLE VIII—VALUES OF COEFFICIENTS FOUND FOR EQUATION: $\Delta$ CHOL. $= b\Delta S + c\Delta M + d\Delta P$ AND FOR THIS EQUATION OMITTING TERM FOR $\Delta M$ (I.E., $c = 0$)

| Line no. | Data used | No. of comparisons | $b$ | $c$ | $d$ |
|---|---|---|---|---|---|
| 1 | Series JWX .. | 10 | 2·91 | −0.11 | −1·28 |
| 2 | Total of 9 series.. | 41 | 2·73 | 0·01 | −1·31 |
| 3 | Series JWX .. | 10 | 2·87 | 0 | −1·27 |
| 4 | 8 Other series .. | 31 | 2·68 | 0 | −1·31 |
| 5 | Total of 9 series.. | 41 | 2·74 | 0 | −1·31 |

Note that, for the construction of the figure, the direction of dietary comparison in each case was chosen so as to provide positive values for observed $\Delta$ Chol. Subtracting the diets in the opposite direction would yield a corresponding figure running down into the lower left-hand quadrant of the X-Y plot.

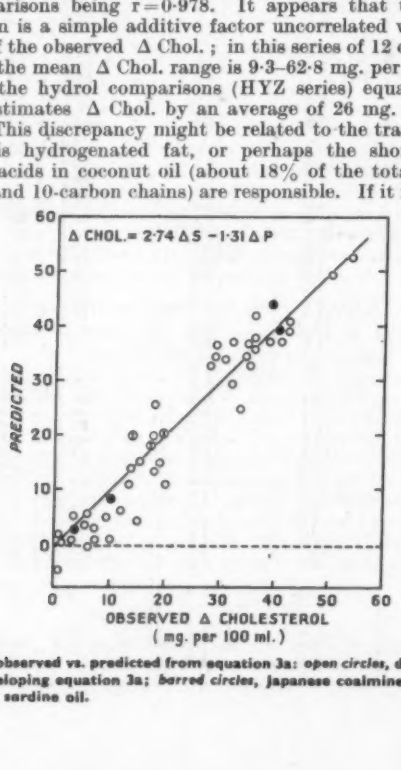
The figure also shows, as barred circles, the application of equation 3a to the 3 sets of data from the Shime experiment and, as solid circles, the 4 comparisons of "sardine" oil with other fats and oils (excluding corn oil). The results of these 7 comparisons are all satisfactorily predicted from equation 3a.

However, test with 12 comparisons involving corn oil shows that equation 3a consistently overestimates the cholesterol values on the corn-oil diet by an average value of 11·0 mg. per 100 ml. (S.E. $= \pm 0{\cdot}89$). The least-squares regression equation for estimating the observed $\Delta$ Chol. in a corn-oil diet comparison from the predicted value from equation 3a is:

$$\text{Observed } \Delta \text{ Chol.} = 11{\cdot}53 + 0{\cdot}97 \text{ (predicted } \Delta \text{ Chol.)}$$

In other words, the average fall in serum-cholesterol level in changing from butter-fat, house, low-fat, olive oil, cotton-seed oil, or sunflower-seed oil to corn oil can be estimated by calculating the predicted value from equation 3a, multiplying by 0·97, and adding 11·53 mg. per 100 ml. The observed serum-cholesterol values are highly correlated with the (uncorrected) values predicted from equation 4, the coefficient of correlation for the 12 comparisons being $r = 0{\cdot}978$. It appears that the correction is a simple additive factor uncorrelated with the size of the observed $\Delta$ Chol.; in this series of 12 observations the mean $\Delta$ Chol. range is 9·3–62·8 mg. per 100 ml.

In the hydrol comparisons (HYZ series) equation 3a overestimates $\Delta$ Chol. by an average of 26 mg. per 100 ml. This discrepancy might be related to the trans acids in this hydrogenated fat, or perhaps the short-chain fatty acids in coconut oil (about 18% of the total being in 8- and 10-carbon chains) are responsible. If it is taken




**$\Delta$ Chol. observed vs. predicted from equation 3a: *open circles*, data used in developing equation 3a; *barred circles*, Japanese coalminers; *solid circles*, sardine oil.**

that the term "saturated acids" for the present purpose refers to fatty acids with chain lengths of 12 or more carbon atoms, the value for S in hydrol is decreased, as indicated at the bottom of table VI, and computations on this basis with equation 3a gives good agreement. In the 3 hydrol comparisons (HYZ in table VII) the observed values for $\Delta$ Chol. are −11·0, −43·3, and −46·1, and the predicted values from equation 3a, only fatty acids of 12 or more carbons being considered, are −9·8, −46·5, and −46·6 respectively. Applying the same convention regarding chain length to all the comparisons in table VII does not change any of the other results appreciably.

### Prediction from only Total Fat and Iodine Values

In many situations it is easier to obtain information about the total fat content of diets and the average iodine value than to estimate the amounts of the several classes of fatty acids. Can this more limited information serve for prediction of $\Delta$ Chol.? It is obvious that diets containing large amounts of fish oils would not fit in any such scheme because the higher degrees of unsaturation of the fish oils beyond the dienes does not seem to be reflected in the serum-cholesterol level (Keys et al. 1957a). But for other ordinary food fats the iodine value of a mixture is related to the proportions of saturated, monoethenoid, and polyethenoid fatty acids in a fairly uniform way. If the average chain lengths of the groups of fatty acids is 18 carbons, and if the polyethenoid fatty acids are dienes (linoleic acid), we have the formula:

TABLE IX—RELIABILITY OF PREDICTION OF SERUM-CHOLESTEROL RESPONSE ($\Delta$ CHOL.) TO CHANGE IN DIET FATS INDICATED BY AVERAGE OF DISCREPANCIES (DISREGARDING SIGN) BETWEEN OBSERVED $\Delta$ CHOL. AND $\Delta$ CHOL. PREDICTED FROM S AND P FATTY ACIDS

(3A) $\Delta$ Chol. $= 2{\cdot}74\Delta S - 1{\cdot}31\Delta P$, and $\Delta$ Chol. predicted from total fat (F) and iodine value (J)

(5) $\Delta$ Chol. $= 73{\cdot}6(F_1/J_1 - F_2/J_2)$.

All values in mg. of Cholesterol per 100 ml.

| Prediction from | Average discrepancy | S.D. | S.E. |
|---|---|---|---|
| 1. Equation 5 .. .. | 9·84 | ±6·80 | ±1·06 |
| 2. Equation 3a .. | 3·65 | ±2·94 | ±0·46 |
| 3. Difference line 1–line 2 .. | 6·19 | .. | ±1·16 |

$$\text{Iodine value} = 86\ M' + 173\ P', \quad (4)$$

where $M'$ and $P'$ refer to the proportions of these acids (as glycerides) in the total fat. With most ordinary diets, including low-fat diets and diets with added ordinary food fats, equation 4 is a good approximation. We have found good agreement between the iodine value computed in this way and that measured directly on the mixed fats extracted from an ordinary house diet.

Accordingly it may be suggested that, as a simple approximation, the serum-cholesterol level should tend to be directly proportional to the amount of dietary fat and its average degree of saturation (or inversely related to the degree of unsaturation). And when the diet is changed, we might have:

$$\Delta \text{ Chol.} = k(F_1/J_1 - F_2/J_2), \quad (5)$$

where F is the amount of total fat, J the iodine value of that fat, and $k$ a constant. For convenience we can express F as the percentage of total calories provided by fats.

To test this equation we have obtained the value for $k$ for the same 41 sets of dietary differences and observed $\Delta$ Chol. values we used in obtaining equation 3a. The mean value of $k$ was 73·60, with a standard error of ±7·38. When this value is substituted in equation 5 and the equation is applied to the 41 sets of experimental

data, the mean discrepancy between observed and predicted values for Δ Chol. proves to be almost three times as large as found in the application of equation 3a to the same data. The computations are summarised in table IX.

The iodine value and total fat, expressed in equation 5, however, do have predictive value, as shown by the coefficient of correlation between Δ Chol. predicted from it and Δ Chol. observed: r=0·899. The corresponding correlation involving Δ Chol. predicted from equation 3a is r=0·978.

The reason for the limited reliability of the computation using iodine values is clear if we consider the coefficients in equations 2b and 3a. If we have two diets with total fats providing 40% of all calories in both cases but the fats are made up of 10%, 80%, and 10% of S, M, and P acids respectively in one case and 40%, 20%, and 40% respectively in the other, the iodine values will be the same. But from equation 2b we would predict that the serum-cholesterol level would be higher on the second diet by 17·2 mg. per 100 ml., since $S_1=4$, $S_2=16$, $P_1=4$, $P_2=16$, so $\Delta \text{Chol.}_{1\text{-}2}=2{\cdot}71\ (12)-1{\cdot}31\ (12)=17{\cdot}2$.

## Discussion

The prediction equations developed here apply only to the conditions of these experiments—namely, adult men aged 30–55, in calorie equilibrium, and with a constant rate of energy expenditure, who are consuming diets containing 10–40% of calories from fats, with periods on each diet of about two to four weeks. Moreover we are concerned with "control" serum-cholesterol levels less than 300 mg. per 100 ml. on ordinary diets of the type where S is about 18% and P about 4% of total calories. Finally, these predictions are for group averages; the reliability of individual prediction is low because of the intra- and inter-variability noted above and because the magnitude of Δ Chol. for a given dietary change tends to be related to the characteristic serum-cholesterol level of the individual. Larger values for Δ Chol. are found in men with idiopathic hypercholesterolæmia. The magnitude of Δ Chol. from a given change in dietary fat tends to be directly related to the intrinsic serum-cholesterol level on a reference diet—e.g., one in which S=18% and P=4% of calories.

It cannot be stated how well the numerical data which have been developed here, including the values of the coefficients in equations 3a and 5, will apply to other groups of men and in other conditions. There are no published data from experiments elsewhere that conform precisely to the conditions of the present study. After this work was finished the papers of Ahrens et al. (1957) and Malmros and Wigand (1957) appeared. Though the data published in these papers do not allow exact comparison, they seem to be at least in fair agreement with the present results and with equation 3a.

The slightly aberrant results obtained with corn oil merit comment. In experiments on animals Jones et al. (1956) report a cholesterol-depressing factor in corn oil not explained by its fatty-acid composition, and from experiments on 57 men. Beveridge et al. (1957) conclude that at least part of the effect of corn oil in the diet must result from something other than fatty acids. It is significant that Ahrens et al. (1957) could not produce a greater effect with safflower-seed oil on the serum-cholesterol level than with corn oil. Very recently we compared corn oil with safflower-seed oil in 141 university students and found a slightly greater cholesterol depression on the corn-oil diet. Perhaps the sterol content of the corn oil is responsible, as suggested by Beveridge et al. (1957).

The total cholesterol responses to the diet reported here are wholly explained by changes in the β-lipoprotein fraction, and this fraction alone is primarily responsible for the differences observed in comparing populations subsisting on different diets (Anderson and Keys 1956, Keys et al. 1956a, Anderson et al. 1957, Keys et al. 1957b).

As regards population comparisons, the question arises whether the observed differences in mean serum-cholesterol levels can be predicted by applying equation 3a to the dietary data. Most of these dietary data provide only very rough estimates of the proportions of the several classes of fatty acids, but it is clear that the observed Δ Chol. is usually considerably larger than would be predicted from equation 3a. The signs and relative values of Δ Chol. are in general agreement, but the magnitude is something like twice what would be predicted from these experiments. The most reasonable explanation is that maintenance for many years on a diet produces larger effects than result in a few weeks or months.

The experiments reported here clearly indicate that the saturated fatty acids, at least those of chain length longer than 10 carbons, have about twice as much effect in raising the serum-cholesterol level as the cholesterol depressing effect of an equal amount of polyethenoids or linoleic acid. This being so, it is not surprising that it is indicated that monoethenoids (oleic acid) have relatively little effect on the serum-cholesterol level. But that oleic acid has absolutely no effect, as indicated in the derivation of equation 3a, cannot be concluded with certainty, because in most of the diets the variation in oleic acid is correlated to some extent with variations in the saturated fatty acid. Experiments are now in progress that should settle the oleic-acid question.

In any case it appears that the speculation that hypercholesterolæmia is simply a manifestation of a deficiency of "essential" fatty-acids (Sinclair 1956) cannot be supported. An excess of saturated fatty acids in the diet seems to explain the high serum-cholesterol levels in populations subsisting on luxurious American and European diets. To lower the serum-cholesterol level adequately a decrease in the intake of saturated fats seems to be more important than an increase in linoleic or other polyethenoids. The mere addition to the diet of small amounts of fats very rich in linoleic acid can have very little effect, and the addition of amounts adequate to have a real effect means an undesirable increase in calories. Fortunately, substitution of one type of fat for the other is both effective and acceptable for dietetic practice.

## Summary

Groups of 12 to 27 men at a time were studied in calorie balance in dietary experiments controlled so that each man was maintained for 4 weeks of standardisation and then for 2–9 weeks on each of 2–6 diets differing in fat content, covering the range of 9–44% of calories from fats, with an experimental fat usually representing about three-fourths of the total fat. Fats studied included butter-fat, hydrogenated coconut oil (hydrol), olive oil, cotton-seed oil, corn oil, sunflower-seed oil, safflower oil, fish oil (*Sardinops cærulea*), and the mixed food fats of ordinary American diets. The intakes of fats, as percentages of total calories provided from glycerides of saturated (S), monoethenoid (M), and polyethenoid (P) fatty acids, were estimated for each man on each diet.

Statistical analysis of the serum-cholesterol levels at the end of each dietary period yielded the least-squares multiple regression equation for the averages of groups of subjects:

$$\Delta \text{Chol.}=2{\cdot}74\Delta S-1{\cdot}31\Delta P,$$

where Δ Chol. is the average change in mg. of total cholesterol per 100 ml. of serum predicted from the changes in the diet in S and in P, for all fats save corn oil and hydrol. The equation overestimates by an

average of 11 mg. per 100 ml. the serum-cholesterol level on diets providing 20–30% of calories from corn oil. The equation is satisfactory in hydrol comparisons if S is interpreted to mean only fatty acids with more than 10 carbons.

Prediction of Δ Chol. can also be made, but with less accuracy, from:

$$\Delta \text{ Chol.} = 73{\cdot}6(F_1J_1 - F_2/J_2),$$

where F is the percentage of total calories from all fats and J is the mean iodine value of those fats. With the group averages from 41 sets of dietary comparisons the average discrepancy between Δ Chol. observed and that predicted from this equation was $9{\cdot}84 \pm 1{\cdot}06$ mg. per 100 ml. The corresponding averaging discrepancy in S and P was $3{\cdot}65 \pm 0{\cdot}46$ mg. per 100 ml.

These equations are much more reliable for groups of men than for individuals because of spontaneous inter- and intra-individual variability.

These experiments and their analysis offer no support for the suggestion that a deficiency of essential fatty acids produces the high serum-cholesterol levels characteristic of populations subsisting on luxurious American and Western European diets. Effective correction of these high serum-cholesterol levels involves a decrease in the most common fats in such diets and the secondary substitution of fats high in polyethenoid fatty acids.

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# RESPONSE OF MEGALOBLASTIC ANÆMIA TO PREDNISOLONE

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AN unexpected hæmatological response to prednisolone in a patient with megaloblastic anæmia who was being treated for rheumatoid arthritis led us to investigate the effects of prednisolone on untreated megaloblastic anæmia in eight other patients. In all but one of these its administration was followed by restoration of normoblastic erythropoiesis as seen in bone-marrow films.

## Methods

### *Procedure*

Before prednisolone was given, the chest was radiographed to exclude pulmonary tuberculosis. After a period of observation had confirmed the absence of a spontaneous hæmatological remission, the patients were given 30 mg. of prednisolone daily by mouth in three divided doses. The treatment lasted 3 weeks, except that cases 4 and 7 were treated for a shorter period and case 8 for a longer period. Potassium citrate 1 g. thrice daily was given concurrently. The patients remained in hospital for at least a week after prednisolone had been discontinued, and all were eventually treated with either cyanocobalamin (vitamin $B_{12}$) or folic acid. None had had anticonvulsant therapy.

### *Estimation of Serum-vitamin $B_{12}$*

Cyanocobalamin (vitamin $B_{12}$) was estimated by the microbiological method reported by Girdwood (1954), the test organism being *Lactobacillus leichmannii*. Normal values range from 130 to 750 μμg. per ml.

### *Absorption of $^{56}$Co-labelled Cyanocobalamin*

The fæcal test of Heinle et al. (1952) was used. This involves the measurement of unabsorbed radioactivity in the fæces after an oral dose of 0·5 μg. of labelled vitamin $B_{12}$. A fæcal recovery of less than 55% of the radioactivity given indicates normal absorption. In cases 7 and 8, where an unexpected normal result was obtained, the test was repeated using 1·0 μg. of $^{56}$Co-$B_{12}$; the urinary excretion method (Schilling et al. 1955) was also used in these two patients.

### *Gastric Secretion and Gastric Biopsy*

The augmented histamine test (Kay 1953) was used after the position of the stomach-tube had been checked fluoroscopically. Achlorhydria was considered to be present if the pH of the gastric juice did not fall below 6 after the administration of 0·04 mg. of histamine per kg. body-weight (the injection of histamine was preceded by one of mepyramine maleate). Biopsy was performed with Wood's flexible gastric-biopsy tube (Wood et al. 1949).

### *Folic-acid Absorption Test*

The method used was that of Girdwood (1953, 1956). The patient is first given 5 mg. of folic acid subcutaneously, and then 5 mg. by mouth not less than 24 hours later. If there is malabsorption, the urinary output of folic acid after the oral dose is significantly less than after the injected one. A healthy person absorbs and excretes in the urine more than 1·6 mg. of the 5 mg. oral dose. As this test involves the administration of a therapeutic dose of folic acid it was performed after the response to prednisolone had been ascertained.

### *Fæcal Excretion of Fat*

The fat-content of the stools was estimated by the method of van de Kamer et al. (1954). The fæcal excretion of fat was measured over 5 or more days, the patient receiving the ordinary ward diet. By this method the mean daily fæcal excretion of fat rarely exceeds 6 g. in a healthy person (Cooke 1956). Where there was evidence of small intestinal dysfunction, the patient received a diet of known fat-content.

### *Estimation of Serum-iron*

The first evidence of the response of megaloblastic anæmia to cyanocobalamin or to folic acid is a fall in the serum-iron level within the first 48 hours of successful therapy (Hawkins 1955). In this series the serum-iron level was estimated in eight patients immediately before prednisolone therapy and at 24 and 48 hours after it had begun; thereafter the level was estimated about weekly. The method of Ramsay (1953) was used, and normal values ranged from 80 to 250 μg. per 100 ml.

## Addisonian Pernicious Anæmia

### FIRST CASE

A single woman, aged 69, had had transient episodes of faintness for 12 months. She had been admitted to hospital 7 months previously with infective hepatitis, and more recently with left basal pneumonia. From both illnesses she had made a good recovery. Her diet was satisfactory, and there was no history of diarrhœa. Apart from pallor of the mucosæ and mild atrophic glossitis, physical examination was negative.

*Investigation.*—Hæmoglobin, 6·6 per 100 ml.; red cells, 1,630,000 per c.mm.; white cells, 4400 per c.mm.; packed-cell volume (P.C.V.), 18·5%; mean corpuscular volume (M.C.V.), 114 c.μ; mean corpuscular hæmoglobin concentration (M.C.H.C.), 35·7%. Bone-marrow megaloblastic. Augmented histamine test: achlorhydria. Gastric biopsy: gastric atrophy. Serum-cyanocobalamin < 50 μμg. per ml. (low). Cyanocobalamin-absorption test: after 0·5 μg. of $^{56}Co$-$B_{12}$, 87% fæcal recovery, or 0·07 μg. of $^{56}Co$-$B_{12}$ absorbed (impaired absorption). Fæcal excretion of fat: 3·6 g. daily (mean of 7 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 2·97 mg.; after 5 mg. orally, 2·56 mg. (normal absorption). Barium meal: no demonstrable abnormality of œsophagus, stomach, or duodenum. Serum-bilirubin, 1·8 mg. per 100 ml. Alkaline phosphatase, 13 King-Armstrong units; cephalin cholesterol flocculation, + 3; thymol turbidity, 2 units; plasma-albumin, 4·1 g. per 100 ml.; plasma-globulin, 2·3 g. per 100 ml.; and non-protein nitrogen, 31 mg. per 100 ml.

The *hæmatological response to prednisolone* (fig. 1 and table) consisted of a suboptimal reticulocyte response followed by a slow rise in the red-cell count and hæmoglobin continuing for 4 weeks after the cessation of treatment. On the 7th day the bone-marrow still contained megaloblasts, though much fewer, and on the 22nd day erythropoiesis was entirely normoblastic. There was no immediate fall in the serum-iron level, and the serum-cyanocobalamin level remained low throughout treatment with prednisolone.

*Summary.*—Addisonian pernicious anæmia responding to prednisolone.

### SECOND CASE

A male supervisor in a gas-works, aged 41, with 2 years' history of increasing lassitude and dyspnœa on exertion had been taking an adequate diet and had no history of diarrhœa. He had atrophy of his lingual papillæ, pale mucosæ, and the auscultatory signs of mitral stenosis. There were no neurological features and no signs of congestive cardiac failure.

*Investigation.*—Hb, 8·9 g. per 100 ml.; red cells, 2,310,000 per c.mm.; white cells, 6600 per c.mm.; P.C.V., 23·5%; M.C.V., 102 c.μ; M.C.H.C., 37·9%. Bone-marrow megaloblastic. Augmented histamine test: achlorhydria. Gastric biopsy: atrophic gastritis. Serum-cyanocobalamin < 50 μμg. per ml. (low). Cyanocobalamin-absorption test: after 0·5 μg. of $^{56}Co$-$B_{12}$, 98% fæcal recovery or 0·01 μg. of $^{56}Co$-$B_{12}$ absorbed (impaired absorption). Fæcal excretion of fat: 5·6 g. daily (mean of 7 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 3·05 mg.; after 5 mg. orally, 2·02 mg. (normal absorption).

The *hæmatological response to prednisolone* is shown in the table. On the 6th day of therapy a further cyanocobalamin-absorption test was made, 0·5 μg. of $^{56}Co$-$B_{12}$ being given three-quarters of an hour after the 10 mg. morning dose of prednisolone. There was no significant improvement in absorption of cyanocobalamin, the fæcal recovery again being high (85% or 0·07 μg. of $^{56}Co$-$B_{12}$ absorbed).

*Summary.*—Addisonian pernicious anæmia with a hæmatological response to prednisolone. Failure of prednisolone to cause significant improvement in the absorption of labelled cyanocobalamin.

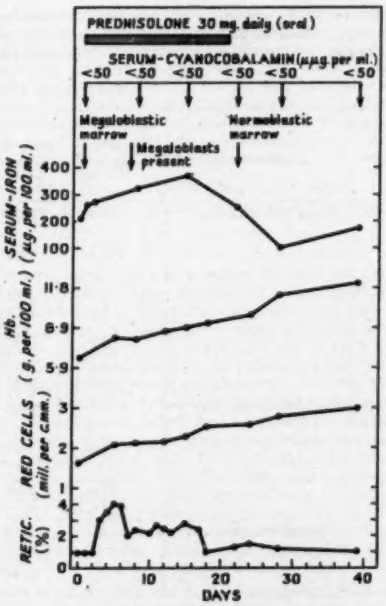


**Fig. 1—Case 1: response of addisonian pernicious anæmia to prednisolone.**

### THIRD CASE

A housewife, aged 65, had for about 8 months had lassitude, dyspnœa on exertion, glossitis, anorexia, loss of weight, and paræsthesiæ. She had been taking a normal diet and had no history of diarrhœa. There were no detectable abnormalities on neurological examination and no significant findings on general physical examination.

*Investigation.*—Hb., 8·9 g. per 100 ml.; red cells, 2,180,000 per c.mm.; white cells, 5000 per c.mm.; P.C.V., 23·5%; M.C.V., 105 c.μ; M.C.H.C., 37·9%. Bone-marrow megaloblastic. Augmented histamine test: achlorhydria. Gastric biopsy: gastric atrophy. Serum-cyanocobalamin < 50 μμg. per ml. (low). Cyanocobalamin-absorption test: after 0·5 μg. of $^{56}Co$-$B_{12}$, 94% fæcal recovery or 0·03 μg. $^{56}Co$-$B_{12}$ absorbed (impaired absportion). Fæcal excretion of fat: 3·2 g. daily (mean of 6 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 2·0 mg.; after 5 mg. orally, 1·8 mg. (normal absorption).

The *hæmatological response to prednisolone* is shown in the table. 5 weeks after this treatment had been stopped, signs of subacute combined degeneration of the cord appeared: there was loss of vibration sense in the lower limbs below the knees, a mild degree of rombergism, and slight exaggeration of the deep reflexes in the right lower limb. The neurological features slowly cleared after intensive treatment with cyanocobalamin.

*Summary.*—Addisonian pernicious anæmia responding to prednisolone. Features of subacute combined degeneration of the cord appeared 5 weeks after the cessation of therapy; this responded to cyanocobalamin.

### FOURTH CASE

A woman, aged 60, who had had rheumatoid arthritis for 28 years, gave a short history of upper abdominal discomfort, anorexia, loss of the sense of taste, loss of weight and lassitude. Her diet was satisfactory and there was no history of diarrhœa. She had been investigated in a chest unit 2 years previously because of recurrent hæmoptysis, and bronchiectasis was diagnosed. She had a family history of pernicious anæmia in two sisters. Despite extensive joint deformities, she was still ambulant. Her rheumatoid arthritis was in an inactive phase. She had atrophic glossitis, and her liver was palpable 6 cm. below the costal margin. There was no neurological abnormality.

*Investigation.*—Hb, 5·9 g. per 100 ml.; red cells, 2,060,000 per c.mm.; white cells, 6000 per c.mm.; P.C.V. 19·5%; M.C.V., 95 c.μ; M.C.H.C., 30·3%; erythrocyte-sedimentation rate (E.S.R.), 45 mm. in the first hour (Westergren). Bone-

marrow megaloblastic. Augmented histamine test: achlorhydria. Gastric biopsy: atrophic gastritis. Serum-cyanocobalamin < 50 μμg. per ml. (low). Cyanocobalamin-absorption test: after 0·5 μg. of $^{58}Co$-$B_{12}$, 80% fæcal recovery or 0·10 μg. of $^{58}Co$-$B_{12}$ absorbed (impaired absorption); and after 0·5 μg. of $^{58}Co$-$B_{12}$ plus 50 mg. intrinsic-factor preparation, 38%

RESPONSE TO PREDNISOLONE IN MEGALOBLASTIC ANAEMIA

| Case no. | Diagnosis | Day | Hb. (g. per 100 ml.) | Red cells (mill. per c.mm.) | Reticulocytes (%) | Bone-marrow | Serum-iron (μg. per 100 ml.) | Serum-cyanocobalamin (μμg. per ml.) | Treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Prednisolone (mg.) | Route | Day |
| 1 | Pernicious anæmia | 0 | 6·6 | 1·63 | 1·0 | Megaloblastic | 208 | <50 | 30 | Oral | 0–20 |
| | | 1 | .. | .. | .. | .. | 261 | <50 | | | |
| | | 2 | .. | .. | .. | .. | 269 | <50 | | | |
| | | 5 | 8·1 | 2·09 | 4·2 (peak) | .. | .. | .. | | | |
| | | 7 | .. | .. | 2·2 | Megaloblasts present | .. | .. | | | |
| | | 8 | 8·0 | 2·13 | 2·5 | .. | 323 | <50 | | | |
| | | 15 | 8·9 | 2·29 | 2·8 | .. | 368 | <50 | | | |
| | | 22 | .. | .. | 1·3 | Normoblastic | 248 | <50 | | | |
| | | 24 | 9·9 | 2·58 | 1·5 | .. | .. | .. | | | |
| | | 28 | 11·3 | 2·80 | 1·1 | .. | 97 | <50 | | | |
| | | 39 | 12·1 | 2·96 | 1·0 | .. | 170 | <50 | | | |
| | | 53 | 13·0 | 3·22 | 1·0 | .. | 154 | <50 | | | |
| | | 74 | 12·1 | 3·17 | 1·0 | .. | 298 | <50 | | | |
| 2 | Pernicious anæmia | 0 | 8·9 | 2·31 | 1·0 | Megaloblastic | 432 | <50 | 30 | Oral | 0–20 |
| | | 1 | .. | .. | .. | .. | 398 | <50 | | | |
| | | 2 | .. | .. | .. | .. | 394 | <50 | | | |
| | | 5 | 8·9 | 2·18 | 1·5 | .. | .. | .. | | | |
| | | 7 | .. | .. | 3·5 | .. | 420 | <50 | | | |
| | | 12 | .. | .. | 5·5 | Normoblastic | .. | .. | | | |
| | | 14 | 11·5 | 2·68 | 7·0 (peak) | .. | 104 | .. | | | |
| | | 21 | 12·7 | 3·71 | 1·8 | .. | 186 | <50 | | | |
| | | 28 | 12·6 | 3·64 | <1 | .. | 228 | <50 | | | |
| 3 | Pernicious anæmia | 0 | 8·9 | 2·18 | 1·0 | Megaloblastic | 264 | <50 | 30 | Oral | 0–20 |
| | | 1 | .. | .. | .. | .. | 300 | <50 | | | |
| | | 2 | .. | .. | .. | .. | 167 | <50 | | | |
| | | 5 | 9·3 | 2·40 | 4·5 | .. | .. | .. | | | |
| | | 6 | .. | .. | 9·1 (peak) | .. | .. | .. | | | |
| | | 7 | .. | .. | 8·0 | Normoblastic | 224 | <50 | | | |
| | | 13 | 10·7 | 2·56 | 1·2 | .. | 154 | .. | | | |
| | | 20 | 12·4 | 3·33 | <1 | .. | 59 | 60 | | | |
| | | 26 | 13·3 | 3·78 | <1 | .. | 187 | .. | | | |
| | | 41 | 13·8 | 3·70 | <1 | .. | 174 | .. | | | |
| | | 48 | 13·0 | 3·44 | <1 | .. | 92 | <50 | | | |
| | | 58 | 13·0 | 3·64 | <1 | .. | 96 | <50 | | | |
| 4 | Pernicious anæmia and rheumatoid arthritis | 0 | 5·9 | 2·06 | <1 | Megaloblastic | 366 | <50 | 30 | Oral | 0–6 |
| | | 1 | .. | .. | .. | .. | 290 | <50 | | | |
| | | 2 | .. | .. | <1 | .. | 328 | .. | | | |
| | | 6 | 4·9 | 1·72 | <1 | .. | .. | .. | | | |
| | | 7 | .. | .. | 1·0 | Megaloblastic | 300 | <50 | Cyanocobalamin 100 μg. | I.M. | 7 |
| | | 8 | .. | .. | 1·0 | .. | 120 | .. | | | |
| | | 9 | .. | .. | 1·6 | .. | 152 | .. | | | |
| | | 12 | .. | .. | 7·0 (peak) | .. | .. | .. | | | |
| | | 13 | 6·1 | 2·11 | 4·5 | .. | .. | .. | | | |
| | | 33 | 8·1 | 3·30 | <1 | .. | .. | .. | | | |
| | | 42 | .. | .. | .. | Normoblastic | .. | .. | | | |
| | | 83 | 13·2 | 5·08 | <1 | .. | .. | .. | | | |
| 5 | Cœliac disease | 0 | 7·4 | 1·84 | 1·0 | Megaloblastic | 185 | 1500 | Prednisolone 30 | Oral | 0–20 |
| | | 1 | .. | .. | .. | .. | 280 | 1250 | | | |
| | | 2 | .. | .. | 1·4 | .. | 233 | 1500 | | | |
| | | 9 | 6·4 | 1·66 | 5·0 (peak) | .. | .. | .. | | | |
| | | 12 | .. | .. | 3·5 | .. | 152 | 1300 | | | |
| | | 13 | 6·2 | 1·59 | 2·5 | Normoblastic | .. | .. | | | |
| | | 16 | 7·6 | 1·84 | 2·8 | .. | .. | .. | | | |
| | | 20 | 8·1 | 2·34 | 3·2 | .. | 138 | 1100 | | | |
| | | 26 | 10·4 | 2·51 | 1·0 | .. | 142 | .. | | | |
| | | 33 | 10·1 | 2·86 | .. | .. | 148 | .. | | | |
| 6 | Cœliac disease | 0 | 5·0 | 1·56 | 1·0 | Megaloblastic | 250 | .. | 30 | Oral | 0–20 |
| | | 1 | .. | .. | .. | .. | 192 | .. | | | |
| | | 2 | .. | .. | .. | .. | 200 | .. | | | |
| | | 7 | 5·8 | 1·63 | 3·8 | .. | 100 | .. | | | |
| | | 8 | .. | .. | 14·2 (peak) | .. | .. | .. | | | |
| | | 10 | .. | .. | 10·8 | Normoblastic | .. | .. | | | |
| | | 14 | 6·8 | 2·48 | 7·0 | .. | 84 | .. | | | |
| | | 21 | 7·0 | 3·71 | <1 | .. | 140 | .. | | | |
| 7 | Megaloblastic anæmia in rheumatoid arthritis | 0 | 10·4 | 2·70 | <1 | Megaloblastic | 65 | 50 | 30 | Oral | 0–16 |
| | | 1 | .. | .. | .. | .. | 86 | .. | | | |
| | | 2 | .. | .. | .. | .. | 122 | .. | | | |
| | | 7 | 11·2 | 3·03 | 2·2 | Transitional erythroblasts | .. | <50 | | | |
| | | 8 | .. | .. | 2·7 (peak) | .. | .. | .. | | | |
| | | 14 | 13·2 | 3·99 | <1 | .. | 126 | .. | | | |
| | | 21 | 13·6 | 3·61 | <1 | Normoblastic | .. | 60 | | | |
| 8 | Megaloblastic anæmia in rheumatoid arthritis | 0 | 8·9 | 2·42 | <1 | Megaloblastic | 135 | <50 | 30 | Oral | 0–35 |
| | | 7 | 11·4 | 2·96 | 1·8 (peak) | .. | 109 | .. | Dose slowly reduced (and stopped 58th day) | | 36–58 |
| | | 14 | 14·0 | 4·17 | <1 | .. | 129 | .. | | | |
| | | 21 | 13·7 | 4·08 | <1 | Normoblastic | .. | <50 | | | |
| | | 29 | 15·1 | 5·13 | <1 | .. | .. | .. | | | |
| | | 36 | 15·0 | 4·98 | <1 | .. | .. | .. | | | |
| | | 42 | 15·0 | 4·97 | <1 | .. | .. | .. | | | |
| 9 | Megaloblastic anæmia after partial gastrectomy | 0 | 6·4 | 1·90 | <1 | Megaloblastic | 225 | <50 | 30 | Oral | 0–20 |
| | | 1 | .. | .. | .. | .. | 241 | <50 | | | |
| | | 2 | .. | .. | .. | .. | 241 | <50 | | | |
| | | 6 | 6·4 | 1·80 | 1·0 | .. | .. | .. | | | |
| | | 8 | .. | .. | 11·5 (peak) | .. | .. | .. | | | |
| | | 9 | .. | .. | 7·8 | .. | 71 | 80 | | | |
| | | 11 | 8·4 | 2·38 | 7·0 | .. | .. | .. | | | |
| | | 18 | 10·7 | 3·01 | 1·0 | Normoblastic | 103 | .. | | | |
| | | 25 | 10·8 | 3·48 | <1 | .. | 104 | 90 | | | |
| | | 32 | 10·4 | 3·56 | <1 | .. | 138 | 90 | | | |
| | | 39 | 10·7 | 3·61 | <1 | .. | 172 | <50 | | | |

fæcal recovery or 0·31 μg. of $^{56}Co$-$B_{12}$ absorbed (normal absorption). Fæcal excretion of fat: 3·2 g. daily (mean of 8 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously 1·50 mg.; after 5 mg. orally, 1·83 mg. (normal absorption).

*Hæmatological response to prednisolone.*—After 6 days' prednisolone therapy the hæmoglobin level and the red-cell count fell, and the marrow was still frankly megaloblastic (see table). Prednisolone was discontinued at this point and treatment with cyanocobalamin begun. This led to a sub-optimal reticulocyte response followed by a slow rise in the red-cell count and hæmoglobin level. Normal blood levels were eventually achieved.

*Summary.*—Addisonian pernicious anæmia in a patient with rheumatoid arthritis. Absence of hæmatological response to prednisolone: however, this treatment was given for only 6 days. Response to cyanocobalamin.

## Megaloblastic Anæmia due to Intestinal Malabsorption

### FIFTH CASE

A widow, aged 58, was admitted to hospital with anæmia which had not responded to iron given by mouth. She had a recent history of lassitude, dyspnœa on exertion, sore tongue, and loss of weight. She had been taking an adequate diet. During the previous 3 years she had had bronchitis. In childhood she had been away from school for 3 years with diarrhœa and protuberant abdomen. Throughout adult life she had had infrequent attacks of diarrhœa with the passage of pale bulky stools. She was pale and slightly emaciated, with moderate atrophic glossitis, slight finger clubbing, and diffuse rhonchi over both lungs. Abdominal examination was negative. There were no neurological features.

*Investigation.*—Hb, 7·4 g. per 100 ml.; red cells, 1,840,000 per c.mm.; white cells, 5200 per c.mm.; P.C.V., 20%; M.C.V., 109 c.μ; M.C.H.C., 37·0%. Bone-marrow megaloblastic. Augmented histamine test: 10·8 mEq. of hydrochloric acid secreted in the post-histamine hour. Serum-cyanocobalamin, 1500 μμg. per ml. (abnormally high). Cyanocobalamin-absorption test: after 0·5 μg. of $^{56}Co$-$B_{12}$, 25% fæcal recovery or 0·38 μg. of $^{56}Co$-$B_{12}$ absorbed (normal absorption). Fæcal excretion of fat on a diet containing 70 g. of fat: 14·3 g. daily (mean of 8 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 2·8 mg.; after 5 mg. orally, 1·2 mg. (impaired absorption). Oral glucose-tolerance test: flat curve. Prothrombin activity 47% of normal. Radiography of small intestine: dilatation of ileum and distal jejunum with prominence of mucosal folds.

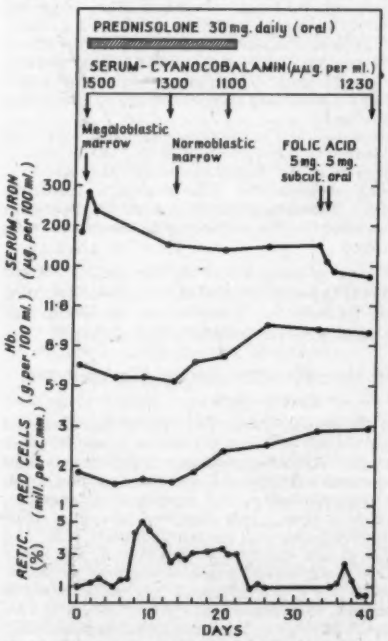


**Fig. 2—Case 5: response of megaloblastic anæmia in cœliac disease to prednisolone.**

The *hæmatological response to prednisolone* is shown in fig. 2 and in the table. The fall in serum-iron level during the 5th week was the result of the administration of 10 mg. of folic acid for an absorption test. Subsequent treatment with folic acid restored the hæmoglobin level and red-cell count to normal. Diarrhœa, which was present when prednisolone therapy was started, ceased two days after the administration of the steroid; this was also accompanied by a fall in the fæcal excretion of fat from 14·3 g. to 8·3 g. daily (mean of 8 days). That the improvement in the steatorrhœa was due to a natural remission cannot be excluded. No cause could be found to explain the abnormally high serum-cyanocobalamin levels, which were confirmed by the *Euglena gracilis* method of assay. There was no clinical or biochemical evidence of hepatic cirrhosis or of malignant disease of the liver. The patient did not have chronic myeloid leukæmia.

*Summary.*—Cœliac disease persisting into adult life with megaloblastic anæmia which responded to prednisolone.

### SIXTH CASE

A married woman, aged 28, was referred from a country district to the blood clinic because of anæmia which had not responded to iron by mouth. For 7 months she had had a sore tongue and for 3 weeks lassitude and dyspnœa on exertion. Immediately before admission she had had an attack of diarrhœa lasting 3 days, but there was no previous history of diarrhœa. Her dietary history was satisfactory. During the previous 4 years she had had occasional episodes of hæmorrhoidal bleeding. The loss of blood had always been slight until 9 days before admission, when she had a profuse hæmorrhage. Between the ages of 4 and 11 years she had been treated elsewhere for rickets; besides the characteristic radiological features of rickets she had had multiple fractures involving the ribs and clavicles. Her renal function was found to be normal, and the rickets was thought to be of dietary origin; the possibility of cœliac disease had apparently not been considered.

She was a small woman with mild residual deformities of rickets in her legs. She had severe atrophic glossitis, her spleen was palpable 4 cm. below the costal margin, and proctoscopy revealed small internal hæmorrhoids.

*Investigation.*—Hb, 5·0 g. per 100 ml.; red cells, 1,560,000 per c.mm.; P.C.V., 16·5%; M.C.V., 106 c.μ; M.C.H.C., 30·3%. Bone-marrow megaloblastic. Augmented histamine test: 0·11 mEq. of hydrochloric acid secreted in the post-histamine hour. Serum-cyanocobalamin: 130 μμg. per ml. (lower limit of normal range). Cyanocobalamin-absorption test: after 0·5 μg. of $^{56}Co$-$B_{12}$, 25% fæcal recovery or 0·38 μg. of $^{56}Co$-$B_{12}$ absorbed (normal absorption). Fæcal excretion of fat on diet containing 70 g. of fat: 2·9 g. daily (mean of 18 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 3·4 mg.; after 5 mg. orally, 0·93 mg. (impaired absorption). Oral glucose-tolerance test: flat curve. Serum-calcium, 9·2 mg. per 100 ml.; inorganic phosphorus, 2·6 mg. per 100 ml.; alkaline phosphatase 8 King-Armstrong units. Prothrombin activity 80% of normal. Radiography of small intestine: normal appearances.

*Hæmatological response to prednisolone.*—To exclude, beyond doubt, a deficiency of cyanocobalamin, this patient had been given cyanocobalamin by injection. After 6 days no change had occurred in either the peripheral blood or the bone-marrow, and prednisolone was then given. The initial response (see table) equalled that which might be expected after treatment with folic acid, but the blood levels soon became stationary—the hæmoglobin after a fortnight, and the red-cell count after 3 weeks. At this stage the red cells were hypochromic. Treatment with ferrous sulphate caused further improvement, but it was not until folic acid had been given that normal blood levels were achieved.

*Summary.*—Cœliac disease persisting into adult life with megaloblastic anæmia that did not respond to cyanocobalamin but responded to prednisolone. Fæcal excretion of fat over a period of 18 days was normal.

## Megaloblastic Anæmia in Rheumatoid Arthritis

### SEVENTH CASE

This was the original patient in whom we observed the response of megaloblastic anæmia to prednisolone.

She was a woman, aged 65, with 16 years' history of rheumatoid arthritis, and was admitted to hospital with exacerbation of joint symptoms. She also had features which suggested mild hypothyroidism, and the findings of a raised plasma-cholesterol and an increased urinary excretion of radioiodine supported this diagnosis. Examination of her blood revealed anæmia with a dimorphic red-cell picture, many of the cells being fully hæmoglobinised and macrocytic while

others were hypochromic. The bone-marrow was megaloblastic. The dietetic history was satisfactory and she had no history of diarrhœa. There were no abnormal neurological features.

The anæmia was partially corrected by blood-transfusion, and treatment with thyroid extract was started. 3 weeks later the marrow was still megaloblastic and, at this stage, a course of prednisolone was given to induce a remission in her joint condition. During the administration of prednisolone, which lasted 6 weeks, her hæmoglobin and red-cell count rose to normal levels and her bone-marrow reverted to normoblastic erythropoiesis. The serum-cyanocobalamin level, estimated on six different occasions, was consistently low. A folic-acid absorption test 10 days before the third marrow examination gave normal results. As this test involved the administration of 10 mg. of folic acid, and as the patient had recently begun treatment with thyroid extract, the hæmatological response could not be ascribed solely to prednisolone.

Normal blood levels were maintained for 2 months after prednisolone had been discontinued. Thereafter there was a gradual fall in the red-cell count and hæmoglobin level, and after a further 2 months the blood findings were: Hb, 10·4 g. per 100 ml.; red cells, 2,700,000 per c.mm.; P.C.V., 32%; M.C.V., 118 c.μ; M.C.H.C., 32·5%; E.S.R., 114 mm. in the first hour. The bone-marrow was again megaloblastic. Other investigations gave the following results. Augmented histamine test: achlorhydria. Gastric biopsy: gastric atrophy. Serum-cyanocobalamin, 50 μμg. per ml. Cyanocobalamin-absorption tests: after 0·5 μg. of $^{56}Co$-$B_{12}$, 47% fæcal recovery or 0·27 μg. of $^{56}Co$-$B_{12}$ absorbed; after 1·0 μg. of $^{56}Co$-$B_{12}$, 48% fæcal recovery or 0·52 μg. of $^{56}Co$-$B_{12}$ absorbed (normal absorption); and after 1·0 μg. of $^{56}Co$-$B_{12}$, and an intramuscular "flushing" dose of 1 mg. of non-radioactive cyanocobalamin 2 hours later, 9·2% urinary recovery (normal absorption). Ability of gastric juice to improve the absorption of $^{56}Co$-$B_{12}$ in patient with addisonian pernicious anæmia: after 0·5 μg. of $^{56}Co$-$B_{12}$ given alone, 95% fæcal recovery or 0·03 μg. absorbed; after 0·5 μg. $^{56}Co$-$B_{12}$ plus 30 ml. of this patient's gastric juice, 54% fæcal recovery or 0·23 μg. absorbed (this suggests intrinsic-factor activity). Fæcal excretion of fat: 3·5 g. daily (mean of 6 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 1·96 mg.; after 5 mg. orally, 1·91 mg. (normal absorption). Oral glucose-tolerance test: normal curve. Barium meal and follow-through examination: no abnormality detected.

A second course of prednisolone was given, and the hæmatological response is shown in the table. On the 7th day the marrow contained many transitional erythroblasts, and on the 21st day erythropoiesis was entirely normoblastic. Subsequent treatment with cyanocobalamin produced a normal red-cell count. The M.C.H.C. remained slightly below normal, and this was attributed to a recurrence in the activity of the rheumatoid disease.

*Summary.*—A case of rheumatoid arthritis with an unusual form of megaloblastic anæmia in that a consistently low serum cyanocobalamin level was accompanied by normal absorption of labelled cyanocobalamin. A hæmatological response during prednisolone therapy could not be attributed with certainty to this drug alone, because other treatment had been given. After 4 months without treatment the bone-marrow was again megaloblastic. A second course of prednisolone produced a hæmatological response with conversion of the bone-marrow to the normoblastic state.

### EIGHTH CASE

A woman, aged 66, who had had rheumatoid arthritis for 26 years was admitted for investigation of macrocytic anæmia. Pernicious anæmia had been diagnosed elsewhere 9 years previously, but her bone-marrow and gastric secretion had not then been examined. Liver therapy was discontinued 4 years after this diagnosis was made, and at intervals thereafter she was treated for hypochromic anæmia. Shortly before admission iron was given intravenously and the anæmia became macrocytic. The dietary history was satisfactory, there was no glossitis, and there was no history of diarrhœa. Both ankle-jerks were diminished, and vibration sense was absent in the legs to the level of the anterior superior iliac spines. There were no other sensory abnormalities and no signs of pyramidal-tract involvement. The rheumatoid arthritis was active.

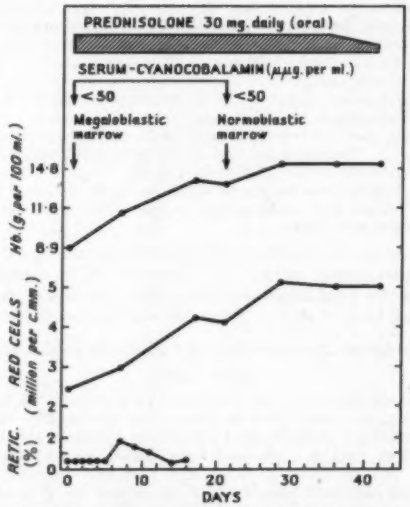


**Fig. 3—Case 8: response of megaloblastic anæmia in rheumatoid arthritis to prednisolone.**

*Investigation.*—Hb, 8·9 g. per 100 ml.; red cells, 2,420,000 per c.mm.; P.C.V., 27%; M.C.V., 112 c.μ; M.C.H.C., 33·0%; E.S.R., 82 mm. in the first hour. Bone-marrow megaloblastic. Augmented histamine test: achlorhydria. Gastric biopsy: gastric atrophy. Serum-cyanocobalamin < 50 μμg. per ml. (low). Cyanocobalamin-absorption tests: after 0·5 μg. of $^{56}Co$-$B_{12}$, 50% fæcal recovery or 0·25 μg. of $^{56}Co$-$B_{12}$ absorbed; after 1·0 μg. of $^{56}Co$-$B_{12}$, 55% fæcal recovery or 0·45 μg. of $^{56}Co$-$B_{12}$ absorbed (normal absorption); and after 1·0 μg. of $^{56}Co$-$B_{12}$ and an intramuscular "flushing" dose of 1 mg. non-radioactive cyanocobalamin given 2 hours later, 6·8% urinary recovery (normal absorption). Ability of gastric juice to improve the absorption of $^{56}Co$-$B_{12}$ in patient with addisonian pernicious anæmia: after 0·5 μg. of $^{56}Co$-$B_{12}$ given alone, 85% fæcal recovery or 0·08 μg. of $^{56}Co$-$B_{12}$ absorbed; after 0·5 μg. of $^{56}Co$-$B_{12}$ plus 35 ml. of the patient's gastric juice, 66% fæcal recovery or 0·17 μg. absorbed (this suggests intrinsic-factor activity). Fæcal excretion of fat: 2·1 g. daily (mean of 8 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 3·0 mg.; after 5 mg. orally, 2·4 mg. (normal absorption). Oral glucose-tolerance test: normal curve. Barium meal and follow-through examination no abnormality detected.

*Hæmatological Response to Prednisolone.*—Prednisolone was given for a longer period in this case than in any of the others, and, as will be seen from fig. 3 and the table, this led to a complete hæmatological remission. The neurological features remained unchanged throughout prednisolone therapy and showed no improvement after subsequent treatment with cyanocobalamin.

*Summary.*—A case of long-standing rheumatoid arthritis with an unusual type of megaloblastic anæmia similar to that observed in case 7. Restoration of blood and bone-marrow to normal after prednisolone therapy.

## Megaloblastic Anæmia after Partial Gastrectomy

### NINTH CASE

A woman, aged 58, gave a history of bouts of diarrhœa and vomiting following partial gastrectomy for a duodenal ulcer 19 months previously. After an initial loss of 20 lb. her weight had remained constant. In recent months she had complained of dizziness, palpitation and dyspnœa on exertion, lassitude, and a sore tongue. Her diet was adequate. She had undergone cholecystectomy 2 years previously. She had atrophic glossitis and her spleen was palpable 3 cm. below the costal margin. Neurological examination was negative.

*Investigation.*—Hb, 6·4 g. per 100 ml.; red cells, 1,900,000 per c.mm.; white cells, 4200 per c.mm.; P.C.V., 19%; M.C.V., 100 c.μ; M.C.H.C., 33·7%. Bone-marrow megaloblastic. Augmented histamine test: achlorhydria. Gastric biopsy: failure to obtain gastric mucosa. Serum-cyanocobalamin

< 50 μμg. per ml. (low). Cyanocobalamin-absorption tests: after 0·5 μg. of $^{58}Co$-$B_{12}$, 80% fæcal recovery or 0·10 μg. of $^{58}Co$-$B_{12}$ absorbed (impaired absorption); after 0·5 μg. of $^{58}Co$-$B_{12}$ with 50 mg. intrinsic-factor preparation, 17% fæcal recovery or 0·42 μg. of $^{58}Co$-$B_{12}$ absorbed (normal absorption). Fæcal excretion of fat: 4·4 g. daily (mean of 5 days). Folic-acid absorption test: urinary output, after 5 mg. subcutaneously, 2·05 mg.; after 5 mg. orally, 2·4 mg. (normal absorption). Barium meal: normally functioning stoma resulting from partial gastrectomy.

The hæmatological response to prednisolone is shown in fig. 4 and in the table.

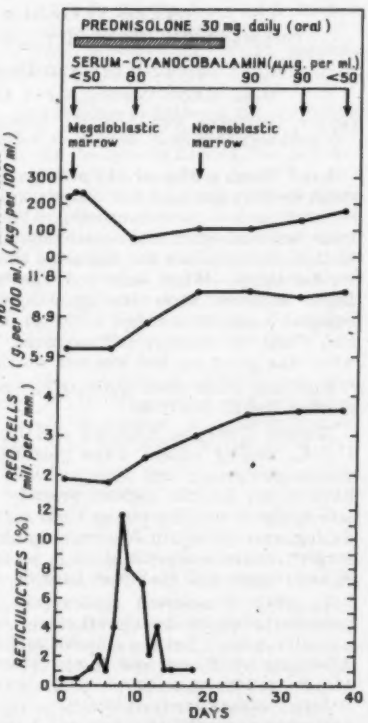


**Fig. 4—Case 9: response of megaloblastic anæmia after partial gastrectomy to prednisolone.**

*Summary.*—Megaloblastic anæmia which developed surprisingly rapidly after partial gastrectomy. There was a hæmatological response to prednisolone.

## Discussion

It is evident from these results that prednisolone given by mouth can produce a hæmatological response in certain forms of megaloblastic anæmia. It must be emphasised that we do not recommend that prednisolone should be used in the treatment of any form of megaloblastic anæmia. The importance of these results must be regarded as mainly theoretical. The hæmatological response obtained in our patients differed in several respects from that which follows treatment with cyanocobalamin or with folic acid. In general, there was a slower rise in the red-cell count and hæmoglobin level, the reticulocyte response was suboptimal, and the initial fall of the serum-iron level constantly seen in the first 48 hours of successful treatment with cyanocobalamin or with folic acid was not observed.

The fact that prednisolone was effective in folic-acid deficiency (cases 5 and 6) as well as in cyanocobalamin deficiency suggests that the therapeutic effect is not due to prednisolone possessing intrinsic-factor activity. This view is further supported by the finding that prednisolone did not significantly improve the absorption of labelled cyanocobalamin in a patient with addisonian pernicious anæmia (case 2). The presence of a known hæmopoietic factor in the prednisolone tablets could explain these results. However, microbiological assay of the tablets with *Streptococcus fæcalis* and *L. leichmannii* as test organisms gave no indication that they contained folic acid, folinic acid, or cyanocobalamin. Thus the results of these initial experiments did not explain our clinical results. Since the precise metabolic roles of cyanocobalamin and folic acid in converting megaloblastic to normoblastic blood formation are uncertain (Girdwood 1957), little purpose would be served by speculating on the metabolic activity of prednisolone in this respect.

The patients with rheumatoid arthritis merit special comment. Case 4 had all the diagnostic criteria of addisonian pernicious anæmia and did not respond to prednisolone. This failure to respond may have been due to the drug not having been given for long enough; but it should be noted that the marrow was still megaloblastic on the 7th day when treatment with cyanocobalamin was begun.

Cases 7 and 8 responded to prednisolone and are of particular interest. Though both presented most of the diagnostic features of addisonian pernicious anæmia (macrocytic anæmia, megaloblastic bone-marrow, achlorhydria, atrophy of the gastric mucosa, and a low serum-cyanocobalamin level), they differed in one important respect—namely, their ability to absorb normal quantities of labelled cyanocobalamin. The gastric juice of each of these patients caused some improvement in the absorption of labelled cyanocobalamin in patients with pernicious anæmia, suggesting intrinsic-factor activity. Detailed dietary studies showed no evidence of a deficient intake of cyanocobalamin, and investigations did not show any disorder of small-bowel function. In both cases the amount of cyanocobalamin absorbed was at the lower limit of our normal range, and the possibility arises that this may actually represent a mild degree of malabsorption of cyanocobalamin. So slight an impairment of absorption of cyanocobalamin would be unlikely to cause megaloblastic anæmia. We have not yet encountered a case of addisonian pernicious anæmia in which the amount of labelled cyanocobalamin absorbed is equal to that found in cases 7 and 8, and we have been unable to find any published reference to such cases. Though it is possible that these patients will eventually develop frank impairment of cyanocobalamin absorption, and would then justifiably be considered as cases of addisonian pernicious anæmia, this stage has not yet been reached despite a low serum-cyanocobalamin level and megaloblastic marrows. For this reason we think it probable that the rheumatoid disease has in some unknown manner precipitated the cyanocobalamin-deficiency state; we have therefore avoided the diagnosis of addisonian pernicious anæmia and at present refer to these patients as having megaloblastic anæmia in rheumatoid arthritis.

In one of the patients with addisonian pernicious anæmia (case 3) evidence of subacute combined degeneration of the cord appeared 5 weeks after the end of treatment with prednisolone; the neurological features slowly cleared after immediate treatment with cyanocobalamin. Though it is possible that this patient would have developed neurological complications at this stage in her illness had she been untreated, the alternative possibility of prednisolone having precipitated the spinal-cord damage must be considered.

Several observations concerning the blood and bone-marrow after the administration of corticotrophin to patients with addisonian pernicious anæmia have been published.

Thorn et al. (1950) give details of a case in which corticotrophin 60 mg. given daily for 8 days produced a reticulocytosis and an increased number of nucleated red cells in the peripheral blood; the red-cell precursors in the bone-marrow changed from a "very immature to a mature type of cell." There was no significant rise in the red-cell count, and the suggestion was made that this may have been a result of the short duration of treatment.

In two patients with addisonian pernicious anæmia, to whom 1250 mg. and 600 mg. of corticotrophin were given in 13 and 8 days, Lowenstein et al. (1951) obtained a partial hæmatological remission of the blood and bone-marrow.

In two further cases (Wintrobe et al. 1951) 675 mg. and 800 mg. of corticotrophin given in 8 and 10 days produced a slight reticulocyte response but no change in the packed-cell volume or in the bone-marrow.

A suboptimal hæmatological response was obtained after corticotrophin therapy in a case of macrocytic anæmia associated with sprue (Glass 1956), while Spies et al. (1955) report two cases of macrocytic anæmia associated with tropical sprue in which a suboptimal hæmatological response followed treatment with prednisone in one case and prednisolone in the other. The bone-marrow findings were not given in any of these three cases.

In conclusion we wish to draw attention to the danger of suppressing the hæmatological evidence of unsuspected megaloblastic anæmia when treating other conditions with prednisolone. In such patients there is the possible additional hazard of precipitating neurological complications.

### Summary

The administration of prednisolone by mouth to nine patients with megaloblastic anæmia produced a hæmatological remission in eight of them. In the patient who did not respond it is possible that treatment was not given for long enough.

The patients comprised four with addisonian pernicious anæmia, two with cœliac disease which had persisted into adult life, two with an unusual form of megaloblastic anæmia associated with rheumatoid arthritis, and one who developed megaloblastic anæmia after partial gastrectomy.

Microbiological assay of the prednisolone tablets did not reveal any folic acid, folinic acid, or cyanocobalamin (vitamin $B_{12}$).

Variable changes took place in the serum-iron level in the first 48 hours of prednisolone therapy, and the fall which constantly occurs at this stage during successful treatment with cyanocobalamin or with folic acid was not observed. There was no significant alteration in the serum-cyanocobalamin levels during prednisolone therapy.

Evidence of subacute combined degeneration of the cord appeared in one of the patients with pernicious anæmia 5 weeks after the end of prednisolone therapy.

We do not consider that steroids should be used as a means of treating megaloblastic anæmia.

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# ATARALGESIA

## OPERATIONS WITHOUT ANÆSTHESIA

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LAST March a 31-year-old primipara was given, by the sister in the ward, an intramuscular injection of pethidine —'Daptazole' (amiphenazole)—'Pacatal.' An hour later, without other medication, she underwent cæsarean section during which she discussed the problem of names for her baby. When delivered, the baby cried at once. Eight minutes after leaving the table, the mother enjoyed a cup of tea and a biscuit, remarking that she had "felt movement, but no pain," that "she knew what was going on, but was not worried."

This and other cases indicate the potentialities of the method I shall describe.

Mushin (1951) in England and Lundy (1957) in the U.S.A., among others, have pleaded for a safe intravenous analgesic; and Dripps (1956) and Slocum (1955) have called for the highest priority to be given for a safe analgesic for disasters and war casualties. Experience during wars shows, in Slocum's opinion, that attempted surgery under analgesia alone is preferable to any type of anæsthesia with its added hazards.

In 1947 I reported satisfactory results for minor procedures under trichlorethylene auto-analgesia from a small inhaler; but the scope of such methods is limited. Attempts by Hewer and Keele (1948), McDermott and Papper (1950), Swerdlow et al. (1955), and others to "push" opiates or their synthetic equivalents to obtund reflexes from severe pain stimuli have failed because a point is reached where analgesia falls off and side-effects proportionately increase (Lasagna and Beecher 1954). On the other hand, pethidine has been established as a supplement to general anæsthesia; by its use, thiopentone requirements are significantly reduced (Auscherman et al. 1956).

Recently, with the advent of opiate antagonists, it has proved possible to increase the dosage of analgesics; and Hamilton and Cullen (1955), and Foldes et al. (1956), for instance, describe the use of antagonist-analgesic mixtures as a supplement to general anæsthesia. Last April Lipson and Bradford (1957) reported operations done without anæsthesia, using (among others) alphaprodine, a short-acting analgesic, along with nalorphine or levallorphan.

The primary object of my own investigations has been to obtain a state of total analgesia safely, consistently, and simply, by using a combination of drugs to produce maximum analgesia with minimum side-effects. Believing that such a state can be achieved only by a combined attack on the body and mind, I suggest for it the name "ataralgesia" (from the Greek *ταραχή*, *tarache*, and *ἀλγέω*, *algeo*, the literal translation being "no disturbance of mind or feeling of pain.")

The criteria for this state are that the patient must be alert, converse intelligently with a voice of normal diction and volume, and cooperate in adjustment of coverings and pillow. Physical tests that may be applied include clipping artery-forceps on the arm, abdomen, and areola of nipple, to which the patient's response should be negligible. (He often feels some pricking or burning sensation; but if he does not see the forceps, the sensation wears off quickly and he remains unconcerned). He must be able to clench his fist 100 times without pain when an inflated cuff on the upper arm occludes circulation. He is never numb: the sensations of touch, pressure, and joint-sense remain. Esmarch tourniquets are felt only as "tight bandages," and cause

no concern. And he must be able to carry on a sensible conversation during and after the operation.

Such a state has been produced in certain patients by the use of a combination of pethidine, amiphenazole, and 'Pacatal.'

The advantages of avoiding anæsthesia are retention of pharyngeal reflexes and lack of depression of other systems. Where unconsciousness is needed, for psychological reasons, a hypnotic can be given solely for this purpose. A possible danger is the masking of shock from visceral stimulation by depression of the withdrawal mechanism. Gentle handling by the surgeon is necessary both for this reason and because the patient is fully aware of what is going on. Undue tension on the tissues may cause breath-catching, phonation, or even slight movement of a hand or head. But it seems that if stimuli do break through, they are of momentary duration, and not distressing.

*Patients.*—The ages ranged from 5 to 73 years, and the weights from 38 to 255 lb. There were as many males as females. Half were European, a quarter Indian and a quarter African. The operations lasted up to four and a quarter hours.

## Investigation

*Drugs.*—During the first phase of my investigation I used morphine and amiphenazole. But my expectation that analgesia would increase proportionately with the dose was not fulfilled. Not only did larger dosage produce respiratory depression, nausea, vomiting, and headaches, but the action of morphine outlasted that of the amiphenazole "cover."

When I substituted methadone or 'Omnopon' for morphine, in the equipotent doses suggested by Keats (1956), the results were no better; and codeine proved weak and depressing. The most satisfactory drug was pethidine.

I then looked for a potentiator or synergist. With promethazine, analgesia was enhanced and surgery had wider scope; but conscious cooperation was too often lost, and postoperative reflexes were sluggish. As others have reported, chlorpromazine was liable, in high doses, to cause peripheral sympathicolytic effects, postoperative mental depression, and intravenous thrombosis. 'Pacatal' proved the best of the drugs I tested, and after trial of its intravenous and intramuscular administration I decided on the latter, which I now use almost exclusively.

The ataralgesic mixture I now employ contains pethidine, amiphenazole, and pacatal. One "unit" of this mixture contains pethidine 100 mg., amiphenazole 25 mg., and pacatal 100 mg. The average adult receives three "units" forty-five minutes before operation. The dose is adjusted for extremes of age and metabolic rates, gross anæmia, shock, and so on. The amiphenazole is dissolved in the pethidine solution, and given intramuscularly; the pacatal is given intramuscularly in a different site.

## Results

Of 78 patients who were given a mixture of pethidine, amiphenazole, and pacatal, operation was done without anæsthetic in 40 (51%). Of these, true ataralgesia was achieved in 15 (see table). These included a school-inspector, aged 53, who wrote his impressions following a repair of ruptured patella tendon under this combination:

"On the operating table I remained conscious and replied to questions all the time . . . very tight bandages, rubber I think, were put on my foot and leg below and above the knee . . . on three occasions, starting before the incision, I felt slight pricks on my left arm and once on my chest [artery-forceps clipped on as tests] . . . I felt a warmish, pricklish, wettish sensation [the incision] but never a painful one, starting what felt to me, some 6 inches above my knee and continuing down to the knee. I had the sensation that there was more than one incision. I felt a number of tugs on my leg, like a needle and cotton being used, and I felt a thump like being hit with a hammer or chisel, but I felt no pain, other than the sensations described. Finally, I felt the tight bandages being released . . . and I said 'Have you finished the operation already?' . . .

"I had been awake all the time, never felt any terror, and felt quite comfortable afterwards. . . . Let me conclude by saying that I had never been before in a hospital, and had never undergone an operation. I dreaded the anæsthetic which would render me unconscious, and I might or might not regain consciousness. However, I agreed to the operation and anæsthetic, and the one given me seemed to calm me, give me confidence, keep me alive and guard me against pain."

SUMMARY OF CASES

| Operations | No. given pethidine, amiphenazole, and pacatal | | Patients in whom true ataralgesia was achieved | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Total | Dose | | Route | |
| | Total | No anæsthetic | Operation | | standard | low | i.m. | i.v. |
| General: | | | | | | | | |
| Intra-abdominal | 9 | 5 | .. | 0 | 0 | 0 | 0 | 0 |
| Extra-abdominal | 6 | 4 | Herniorrhaphy | 1 | 1 | 0 | 1 | 0 |
| Gynæcological: | | | | | | | | |
| Major .. .. | 12 | 6 | Cæsarean section | 4 | 4 | 0 | 3 | 1 |
| Minor .. .. | 11 | 7 | Dilatation and curettage | 3 | 1 | 2 | 2 | 1 |
| Orthopædic: | | | | | | | | |
| Major .. .. | 7 | 3 | Repair of patella | 1 | 1 | 0 | 1 | 0 |
| Minor .. .. | 4 | 3 | | 1 | 1 | 0 | 1 | 0 |
| Plastic .. .. | 7 | 5 | .. | 0 | 0 | 0 | 0 | 0 |
| Ear, nose, and throat | 10 | 2 | Tonsillectomy; submucous resection | 2 | 1 | 1 | 1 | 1 |
| Other: | | | | | | | | |
| Major .. .. | 2 | 1 | .. | 0 | 0 | 0 | 0 | 0 |
| Minor .. .. | 10 | 4 | | 3 | 2 | 1 | 3 | 0 |

25 patients were able to undergo operation without anæsthesia, but were too drowsy to be included in the ataralgesic group. They had such major operations as Wertheim's hysterectomy, thoracotomy, and gastrectomy.

Of the remaining 38 patients given the mixture, there were some who appeared to be in the ataralgesic state but were put to sleep before or after the incision for various reasons.

Where relaxation was necessary, gallamine triethiodide or suxamethonium was used with safety; but ataralgesia alone can produce relaxation of spasm due to pain, as in fractures and dislocations.

In most of the major abdominal cases a smaller proportion of amiphenazole was used. The narcotic effect was thus heavier.

Increments of 1 "unit" were sometimes given intravenously (or intramuscularly with hyaluronidase).

There have been no deaths and no evidence of damage to the liver or bone-marrow.

*Complementary Anæsthesia.*—It has often been propounded that analgesics supplement anæsthetics. I suggest the reverse concept—that anæsthesia should complement analgesia.

In this series thialbarbitone sodium and thiopentone sodium were the only hypnotics used. The average requirement (in those receiving it) was 440 mg. thiopentone per hour. We found that, given *after* thiopentone, our mixture was liable to produce considerable respiratory depression.

Anæsthesia was needed for psychological or technical reasons (e.g., muscular paralysis and controlled respiration), or because of underdosage or break-through of pain.

*Cardiovascular System.*—Tachycardia is usual with the intravenous, and unusual with the intramuscular route; electrocardiograms show sinus tachycardia but no significant abnormality. In 2 patients the pulse became irregular for short periods. Hæmorrhage is almost

always reduced, but the blood-pressure appears stable, and is less disturbed by surgical manipulations (e.g., traction) than one is accustomed to expect. Oligæmic shock is no contraindication; and the clinical impression is that the mixture tends to prevent onset of shock.

*Nervous System.*—Reflexes are, of course, present unless an anæsthetic has been given: so little of this is required that no patient need leave the table without all his reflexes. Recovery is rapid, and no patient has caused anxiety to the nurses. After barbiturate anæsthesia, an occasional patient may remain stuporose (though rousable) for some hours. Postoperative exercises are usually willingly undertaken, and movements are not resented, as the analgesia wears off slowly in the ward. Analgesia lasts two to twelve hours (average about six). Closed plasters must be watched carefully, because the danger signal of ischæmic pain will be absent. No patient has vomited.

Recollection is patchy: after true ataralgesia, patients remember most events, but with no resentment: on the contrary, they seem intrigued, and in written statements recall their remote unconcern. Some can describe many details immediately after operation but, during the next few days forget them.

*Respiratory System.*—Alveolar ventilation fell to 30% after three minutes, following fast intravenous injection, but rose to 70% by the sixth minute and to 90% by the twelfth minute; with intramuscular injection it fell to 80% at the thirtieth minute, and then slowly returned to normal. Using the intramuscular route, oxygen supplementation has not been necessary. Tissue respiration is probably reduced.

*Midwifery.*—In midwifery the combination has been used successfully with no depressant effect on the child.

*Dosage.*—A disadvantage of the method is the large bulk of the injection (6 ml. pethidine + amiphenazole and 12 ml. pacatal). Pacatal often stings on entry, and may leave an aching area for a day or two, but no necrosis or thrombosis has been seen.

The necessary dose is sometimes hard to predict. Alcoholics and those who have taken habit-forming drugs need more, but starvation, and inanition and shock call for lesser doses. With excessively nervous and hyperthyroid patients ataralgesia was not obtained, and even analgesia was often unsatisfactory.

With intramuscular injection the maximum effect is seen in about thirty minutes. The mental outlook is always clearer than after intravenous injection, and the analgesia seems to be of the same order. For oral surgery, where the saliva at times becomes tenacious, atropine gr. $^1/_{100}$ should be given.

The series of 78 administrations of pethidine, amiphenazole and pacatal is too small for detailed analysis, and a fuller report will appear later.

### Discussion

Routine surgery does not often call for the ataralgesic or the purely analgesic state; for most patients prefer to be asleep. Nevertheless such a state has many uses. After accidents patients could be rendered pain-free and cooperative, and be transported and operated upon without further medication (though head, spinal, and abdominal injuries would need careful assessment first). The method described needs improvement, and another method is under study; but it has proved helpful in saving time, admissions, beds, theatre-space, and demands upon anæsthetists. Physicians may perhaps find a use for ataralgesia in cases where their investigations are limited by the barrier of pain.

### Summary

78 patients have been given a mixture of pethidine, amiphenazole ('Daptazole'), and 'Pacatal' to induce a state of "ataralgesia"—i.e., of calmness and freedom from pain. In 40 of these patients operations (some major) were done without anæsthesia. In 15 of these a true state of ataralgesia was obtained. In the remaining 38, very small quantities of intravenous barbiturate were needed.

The benefits of the method are safety, lack of depression of other systems, retention of reflexes, and rapid recovery. When a sleep-dose of barbiturate is required, the term "complementary anæsthesia" is applicable.

No serious drawbacks were encountered; but, though apparently safe, the method used is clearly far from perfect, and alternative means of inducing ataralgesia are being tried.

### ADDENDUM

Since this paper was submitted, figures from the continuation of the pethidine-amiphenazole-pacatal series show improved results. Of a total of 56 (87%) were performed without complementary anæsthesia; and of these 49, 39 (79%) were classified as true ataralgesia.

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## IN-VITRO ACTIVITY OF SIGMAMYCIN

### (A COMBINATION OF TETRACYCLINE AND OLEANDOMYCIN)

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THE tendency of some bacteria, in particular *Staphylococcus aureus*, readily to develop resistance to the standard antibiotics has directed attention not only to the production of new antibiotics but also to the possibility of obtaining enhanced activity by combining antibiotics. Although many attempts have been made to demonstrate synergic activity by various combinations of antibiotics, little convincing evidence of success has been produced. The results have tended to be inconsistent and unpredictable.

English et al. (1956), however, claim that a combination of tetracycline and oleandomycin in the ratio of 2½ 1, known as 'Sigmamycin' or P.A.755, not only shows synergistic activity but also delays the emergence of resistant variants of *Staph. aureus*. Although only a limited number of organisms, mainly *Staph. aureus*, were examined, the results have been received with enthusiasm in some quarters of the U.S.A., and it has been suggested that a new era of combined antibiotic therapy has now arrived (Welsh 1957).

These views have been strongly challenged in the U.S.A. by other authorities who regard the claims as premature and condemn the routine uncontrolled use of fixed combinations of antibiotics. They think that these mixtures are unlikely to produce synergism and can in fact be harmful (Dowling 1957, Finland 1957).

In view of the importance of the claims made for sigmamycin and the conflicting reports about the value

of combinations—particularly predetermined and fixed combinations—of antibiotics, we investigated the in-vitro activity of oleandomycin, tetracycline, and sigmamycin, especially as regards (1) the production of synergic activity and (2) the retarding effect on the emergence of resistant variants.

## Methods

The sensitivity tests were carried out by the standard serial-dilution method.

Doubling dilutions of the antibiotics were prepared in 1·0 ml. of glucose broth, plus indicator, to which 0·02 ml. or one drop (50 drops per ml.) of an overnight broth-culture of the organisms was added. As this was a relatively large inoculum, the technique of English et al. (1957) was also used sometimes: an inoculum of 0·5 ml. of a 1/1000 dilution of an overnight broth-culture was added to 0·5 ml. of broth+antibiotic.

The results were read after incubation at 37°C for 20–24 hours and also, in some cases, for 48–72 hours. The minimal inhibitory concentration was the smallest amount of antibiotic preventing visible growth of the organism. All the organisms had been freshly isolated from a wide variety of human infections.

The antibiotic solutions of tetracycline, oleandomycin, and sigmamycin were prepared in distilled water from special salts provided by Pfizer & Co. Stock solutions (2000 μg. per ml.) were prepared and kept in the refrigerator for not more than a month. Standard solutions of erythromycin were also prepared and examined.

## Results

As there is no generally accepted definition of synergism, and as these tests deal only with in-vitro activity, it is important to define the terms used in expressing the results of the investigation:

*Synergism.*—The activity (minimal inhibitory concentration) of the combination is greater than that of either component alone.

*Interference.*—The activity of the combination is less than that of the more effective of the two antibiotics.

*Additive result.*—The activity of the combination is equal to that of the more effective component.

The 165 organisms examined were divided into four main groups according to their sensitivity to tetracycline and oleandomycin, the component antibiotics of sigmamycin (table I).

Evidence of enhanced activity or synergism was obtained with 44 out of 165 organisms, but in 40 out of 44 instances the organisms were sensitive to both tetracycline and oleandomycin; only on 4 occasions was synergism demonstrated with organisms resistant to one or both antibiotics. The great majority of organisms were gram-positive cocci, and the synergism was of doubtful significance because there was only a twofold, or one-tube, difference between the results given by sigmamycin and the more active component of the combination. This difference was consistent and was usually found on retesting the organisms; nevertheless it is within the recognised limits of experimental error for the test. With 5 organisms a fourfold difference in sensitivity was observed, and on 1 occasion there was an eightfold difference.

TABLE I—BEHAVIOUR OF PATHOGENS TO SIGMAMYCIN AND ITS COMPONENT ANTIBIOTICS

| Strains examined | No. examined | Reaction to sigmamycin | | |
|---|---|---|---|---|
| | | Synergism | Additive | Interference |
| *Oleandomycin-sensitive and tetracycline-sensitive:* | | | | |
| *Staph. aureus* .. .. | 50 | 30 | 18 | 2 |
| *Str. faecalis* .. .. | 10 | 8 | 1 | 1 |
| *Str. pyogenes* .. .. | 3 | 2 | 1 | 0 |
| Pneumococcus .. .. | 4 | 0 | 3 | 1 |
| *Oleandomycin-sensitive and tetracycline-resistant:* | | | | |
| *Staph. aureus* .. .. | 18 | 0 | 2 | 16 |
| *Staph. albus* .. .. | 1 | 6 | 1 | 0 |
| *Str. faecalis* .. .. | 7 | 0 | 3 | 4 |
| *Oleandomycin-resistant and tetracycline-sensitive:* | | | | |
| Coliforms .. .. .. | 25 | 1 | 14 | 10 |
| *Str. faecalis* .. .. | 1 | 1 | 0 | 0 |
| *Oleandomycin-resistant and tetracycline-resistant:* | | | | |
| *Staph. aureus* .. .. | 2 | 0 | 1 | 1 |
| *Staph. albus* .. .. | 2 | 0 | 1 | 1 |
| Coliforms .. .. .. | 9 | 1 | 5 | 3 |
| Proteus .. .. .. | 22 | 1 | 8 | 13 |
| *Ps. pyocyanea* .. .. | 10 | 0 | 6 | 4 |
| *Str. faecalis* .. .. | 1 | 0 | 1 | 0 |
| Total .. .. .. | 165 | 44 | 65 | 56 |

TABLE II—HABITUATION OF SENSITIVE STRAINS (3) OF *Staph. aureus* TO ERYTHROMYCIN, OLEANDOMYCIN, TETRACYCLINE AND SIGMAMYCIN

| Subculture in | —Fold increase in resistance, after 20 subcultures, to | | | |
|---|---|---|---|---|
| | Erythromycin | Oleandomycin | Tetracycline | Sigmamycin |
| Erythromycin .. | >128 | >128 | 0–2 | 0–8 |
| Oleandomycin .. | >128 | >128 | 0–2 | 2–4 |
| Tetracycline .. | 0–2 | 0–2 | 16–64 | 8–16 |
| Sigmamycin .. | 4 | 4 | 4–16 | 4–8 |

In contrast, interference was found with 56 out of 165 organisms, but again this tended to be of doubtful significance, there being usually a twofold difference in the readings. It was found particularly with organisms resistant to one or both antibiotics and was probably a dilution effect.

Even when enhanced activity against *Staph. aureus* was shown by sigmamycin, the minimal inhibitory concentration of this compound was never less than that given by erythromycin alone. Thus a single effective antibiotic was at least as active as the combination.

The size of the bacterial inoculum used in the sensitivity tests did not influence the general trend of the results.

### Habituation to Oleandomycin and Tetracycline

The claim that sigmamycin prevented or delayed the emergence of strains resistant to the two component antibiotics was next examined.

Three sensitive strains of *Staph. aureus* were grown in increasing concentrations of oleandomycin, tetracycline, erythromycin, and sigmamycin. Broth was the medium, and incubation for 2–4 days was allowed between each transfer. Sensitivity tests were made on the three organisms before, during, and after 20 transfers. The organisms reacted in a similar manner (table II).

In all the cases some degree of resistance was induced by growth in subinhibitory concentrations of the homologous antibiotics. Resistance to oleandomycin and erythromycin developed rapidly during growth in the homologous antibiotic, and there was complete cross-resistance between these two antibiotics, resistance developing approximately at the same rate and to a similar degree, but there was little or no change in the reaction to tetracycline or to sigmamycin. Resistance to tetracycline was induced more slowly and to a lesser degree, and there was also an increase in resistance to sigmamycin but little or no change in sensitivity to the two other antibiotics. In the presence of sigmamycin, there were little alteration in the sensitivity to oleandomycin, erythromycin, and sigmamycin and only a moderate increase in resistance to tetracycline. The artificially induced resistance to erythromycin and oleandomycin was not permanent but tended to decrease appreciably on subculturing in antibiotic-free broth.

### Cross-resistance between Erythromycin and Oleandomycin

Many workers report a close relation between erythromycin, oleandomycin, and spiramycin (Jones et al. 1956, Garrod 1957).

During this investigation organisms sensitive to oleandomycin were also sensitive to erythromycin, but erythro-

mycin tended to be two to four times as active, weight for weight, as oleandomycin. Moreover the three strains of *Staph. aureus* rendered resistant in vitro to erythromycin became equally resistant to oleandomycin, and vice versa. Apart from the few strains of *Staph. aureus* naturally resistant to erythromycin, organisms resistant to one antibiotic were also resistant to the other.

Only four erythromycin-resistant strains of *Staph. aureus* were isolated from patients, and these behaved irregularly in the sensitivity tests, in a manner reported by Garrod (1957).

Two appeared to be in the "double" phase and gave definite cross-resistance to oleandomycin. The other two were of the "dissociated" pattern and gave irregular results on repeated testing; consequently they have been omitted from table I. After overnight incubation these strains, though very resistant to erythromycin, appeared to be sensitive to oleandomycin. Sometimes, but not always, strong resistance to oleandomycin developed after further incubation for 24–48 hours.

Apart from these irregularities, erythromycin and oleandomycin had very similar actions. The two antibiotics thus appear to be closely related, but the relation is much more complex than is found between members of the tetracycline group.

A few sensitivity tests were made with a mixture of 2 parts tetracycline and 1 part erythromycin. As the preliminary results were inconclusive and the general trend was similar to that obtained with sigmamycin, the tests were abandoned.

### Discussion

The results of this investigation do not support the widespread claims for the synergic activity by mixtures of tetracycline and oleandomycin in the form of sigmamycin. Indications of synergism were generally of doubtful significance—merely a twofold difference in the results. Moreover this type of reaction was usually given by very sensitive organisms, and the combination is therefore unlikely to be of practical value, because infections with sensitive organisms can be adequately dealt with by a single antibiotic.

In many cases a minor degree of interference or antagonism was observed, particularly with resistant organisms; this seemed to be mainly of a quantitative kind, depending on the dilution of the more active ingredient in the combination. It is therefore possible that, under such conditions, the mixture of antibiotics might be *less* effective therapeutically than a single active agent.

Support was obtained for the contention that the combination of oleandomycin and tetracycline retards the development of resistance in vitro to the individual antibiotics. It cannot, however, be assumed that similar results would follow the clinical application of this mixture, and the practical value is uncertain.

It is difficult to justify the general application of fixed and predetermined combinations of antibiotics in routine practice. Jawetz and Gunnison (1953), who studied synergism in great detail, thought that synergistic or antagonistic pairs of drugs do not exist; the effect on bacteria is unpredictable, and different strains of the same bacterial species may not behave in the same way. The tests made with sigmamycin did not yield any evidence against these views.

Synergism by antibiotics is difficult to demonstrate clinically. In some cases where strong claims for synergic activity by combined antibiotic therapy have been made —e.g., in the treatment of subacute bacterial endocarditis and brucellosis—the causal organisms are relatively inaccessible, and it is impossible to determine how much of the different antibiotics reaches the organisms in situ. Under these conditions the diffusibility of, and penetration by, the antibiotics may well be as important as synergism in effecting a cure.

Combinations of antibiotics should be used with caution and only when there are special indications, clinical or bacteriological. It is necessary to repeat that, with the increasing complexity of the antibiotics, their use should be subjected as far as practicable to laboratory control.

### Summary

Studies of sigmamycin (a combination of 2 parts tetracycline and 1 part oleandomycin) have confirmed claims that the mixture delays in vitro the emergence of resistant variants of *Staph. aureus*.

Attempts to demonstrate consistent and significant synergic activity by this combination in vitro against 165 common pathogens were unsuccessful.

We wish to thank Messrs. C. Pfizer for supplying the special salts of oleandomycin, tetracycline, and sigmamycin.

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## PRECIPITIN TESTS IN THYROID DISEASE

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ANTIBODY to human thyroglobulin has been demonstrated, by means of a precipitin test, in the serum of patients with untreated or recently treated Hashimoto's disease (Roitt et al. 1956). These workers suggest that this might be a useful specific diagnostic test for this condition. The present study was undertaken to determine the prevalence of precipitating antibodies to human thyroid tissue in a large group of hospital patients with many different diseases.

### Methods

Sera were examined by a precipitin test, using thyroid extract as antigen.

To prepare this, thyroid-gland tissue was frozen, finely sliced, and extracted for fifteen minutes with an approximately equal amount of saline solution in a mechanical shaker. The saline extract was centrifuged for fifteen minutes at 3000 r.p.m. to remove most of the suspended material, leaving a clear pink fluid which keeps for at least eight months, without apparent deterioration, when stored at −15°C. For reasons stated below, extracts were diluted 1 in 4 with saline solution before use: accurate standardisation of the amount of antigen in such extracts seems unnecessary and was not attempted.

All the thyroid glands we have studied have provided effective antigens. They include glands removed surgically for thyrotoxicosis or for colloid goitre and normal glands obtained shortly after death.

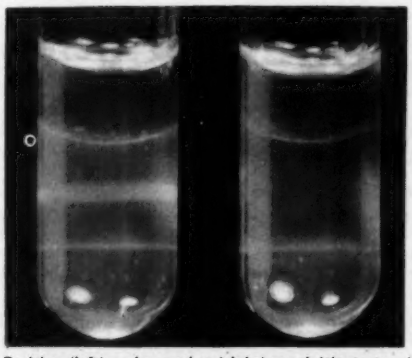

Fig. 1—Positive (left) and negative (right) precipitin tests. (×2.)

After trying several techniques for precipitin tests we adopted a modification of the method described by Oakley and Fulthorpe (1953):

About 0·25 ml. of patient's serum was pipetted into a test-tube measuring 7 mm. × 70 mm., care being taken not to smear the sides of the tube with serum. 0·5% agar, dissolved in 0·9% saline solution containing 0·03% of sodium azide, was melted and cooled to 50°C, and 0·35 ml. was gently floated on to the serum and allowed to set. 0·25 ml. of antigen was then added to lie above the agar. The tube was stoppered, kept at room temperature, and examined daily in a good light against a dark background. A clear-cut layer (so-called ring) of white precipitate developing in the agar layer was regarded as a positive result (fig. 1).

Positive tests almost always showed a well-defined precipitate within seven days; but we have examined all tests for fourteen days before discarding and have encountered one specimen in which a positive test developed only after seven days: this case is discussed below.

An ill-defined turbidity extending upwards from the bottom of the agar layer was sometimes observed, and was not regarded as a positive reaction; this could not be entirely prevented by centrifuging the serum before testing. There is a danger that weak positive reactions may be partly obscured by such non-specific turbidity; for, when the antibody is weak, the zone of precipitation is in the lower part of the agar layer and gradually moves downwards as solution takes place in the antigen-excess zone. Use of a 1 in 4 dilution of the thyroid extract, as described above, raises the level of the zone of precipitation and facilitates the detection of weak reactions.

A slight modification of technique, which was found useful in setting up single or small numbers of tests, was to prepare a stock of tubes, each containing 0·35 ml. of the 0·5% agar: after the agar has been melted, the test serum can be pipetted beneath it, and the test proceeded with as described above.

## Material

Specimens of serum were examined from hospital patients with Hashimoto's disease, thyrotoxicosis, primary myxœdema, simple non-toxic goitre, carcinoma of thyroid, lymphosarcoma of thyroid, and struma reticulosa, and from general medical and surgical patients not regarded as having thyroid disease.

The diagnosis of Hashimoto's disease was made on histological examination of the thyroid gland whenever material was available (15 cases), and here we applied Joll's criteria (1939). We did not feel justified in performing biopsy for the purpose of this investigation, and in the remaining cases diagnosis has depended on the demonstration of serum-protein abnormalities or on characteristic $^{131}I$ findings—methods which have been shown to be of value in confirming the clinical diagnosis of Hashimoto's disease (Luxton and Cooke 1956, Doniach and Hudson 1957). Thus, in our 17 cases without biopsy, diagnosis was based upon the following evidence:

(1) All 17 patients were middle-aged women, either euthyroid or hypothyroid, and with a firm or hard generalised thyroid enlargement.

(2) In 12 patients abnormal serum-flocculation tests or raised serum-γ-globulin levels (or both abnormalities) were found in the absence of overt liver disease.

(3) In 2 patients a state of hypothyroidism was associated with a normal $^{131}I$ uptake and high normal protein-bound $^{131}I$ levels.

(4) 3 patients were shown to fulfil both criteria 2 and 3.

The application of the alternative criteria (2) and (3) was necessitated by the different diagnostic tests made at two clinics from which our patients were drawn. We do not regard the above criteria as being completely satisfactory for the diagnosis of Hashimoto's disease. Even when biopsy material from the thyroid gland is available, the application of Joll's criteria may sometimes be very much a matter of personal opinion. Nevertheless we have tried to adhere strictly to our criteria, and cases in which the diagnosis seemed to us to be in doubt have been excluded: the number is too small to alter significantly the trend of our results.

Our patients with simple non-toxic goitre were clinically euthyroid and were either diagnosed histologically (8 cases) or shown to have normal serum-flocculation tests (9 cases). The cases of malignant disease of thyroid were confirmed histologically. The diagnosis of primary myxœdema was applied to patients who showed definite signs of hypothyroidism and whose thyroid gland was not palpable; any history of goitre or of thyrotoxicosis and any evidence of pituitary insufficiency excluded patients from this group.

## Results

The results of precipitin tests are summarised in table I. Besides presenting the highest proportion of positive tests, the Hashimoto patients also gave, in general, stronger reactions (as judged by the density of precipitation) than did the positive cases of thyrotoxicosis and myxœdema. A few of the positive sera were tested against extracts of human organs other than thyroid gland: in no case was a precipitin reaction observed.

The Ouchterlony plate technique was used to compare the reactions of different sera, and by this method a reaction of identity was observed between different cases of Hashimoto's disease, between Hashimoto's disease and myxœdema, and between Hashimoto's disease and thyrotoxicosis. The serum of 1 of our patients with Hashimoto's disease gave two distinct zones of precipitation, both of which blended, on Ouchterlony plates, with the single zone of other sera. When the Ouchterlony plates are left for several days, it is apparent that more than one zone is present in many of the cases of Hashimoto's disease, and the picture becomes complex. We have not yet observed a reaction of non-identity with any of the zones exhibited by different sera.

## Discussion

These results confirm the observation of Roitt et al. (1956) that precipitating antibodies reacting with thyroid extract are present in the serum in Hashimoto's disease. In view of the difficulty, discussed above, of formulating and applying diagnostic criteria for this disease, caution must be exercised in comparing diagnostic methods in

TABLE I—RESULTS OF PRECIPITIN TESTS IN HOSPITAL PATIENTS WITH VARIOUS CONDITIONS

| Diagnosis | No. of cases tested | No. of positive tests |
|---|---|---|
| Untreated Hashimoto's disease .. | 16 | 12 |
| Treated Hashimoto's disease .. .. | 16 | 8 |
| Primary myxœdema .. .. .. | 28 | 4 |
| Thyrotoxicosis .. .. .. .. | 120 | 3 |
| Simple non-toxic goitre .. .. | 17 | 0 |
| Carcinoma of thyroid .. .. .. | 3 | 0 |
| Lymphosarcoma of thyroid .. .. | 1 | 0 |
| Struma reticulosa .. .. .. | 1 | 0 |
| Patients without thyroid disease .. | 133 | 0 |

TABLE II—CASES OF UNTREATED HASHIMOTO'S DISEASE WITH A NEGATIVE PRECIPITIN TEST

| Case no. | Age (yr.) | Sex | Duration of disease | Thyroid gland | Thyroid status | Serum-flocculation tests | Serum-γ-globulin level | $^{131}I$ studies | Histology |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 49 | F | 12 yr. | Firm, moderate enlargement | Slightly hypothyroid | Abnormal | Raised | Normal | None |
| 2 | 60 | F | 1½ yr. | Firm, moderate enlargement | Euthyroid | Abnormal* | Raised | None | None |
| 3 | 36 | F | 4 yr. | Firm, moderate enlargement | Hypothyroid | Abnormal | Raised | None | None |
| 4 | 64 | F | 9 mos. | Firm, moderate nodular enlargement | Euthyroid | Normal | Raised | None | Hashimoto's disease |

* In this patient the serum-alkaline phosphatase level was 24 King-Armstrong units. There was no clinical or other biochemical evidence of liver disease.

different series of cases. With this reservation in mind, our experience with the precipitin test suggests that it is slightly less sensitive than the serum-flocculation tests and estimation of serum-γ-globulin.

Luxton and Cooke (1956) reported abnormal results of testing the serum with colloidal gold in 21 of 24 patients with Hashimoto's disease who had not been treated with thyroid hormone : the 3 who gave normal results had undergone thyroidectomy, which reverses the results of testing the serum with colloidal gold in Hashimoto's disease (Doniach and Hudson 1957). Skillern et al. (1956) found positive colloidal-gold reactions in 25 of 31 histologically proven cases and raised serum-γ-globulin levels in 22 of 26. In our own series three-quarters of the untreated patients with Hashimoto's disease gave positive precipitin tests, and more direct evidence of lack of sensitivity of the test is provided by 4 cases with raised serum-γ-globulin levels (3 of whom had abnormal flocculation reactions) in whom the precipitin test was negative (table II). In 1 patient proved, at subsequent operation, to have Hashimoto's disease a positive precipitin reaction was obtained while serum-flocculation reactions and the serum-γ-globulin level were normal. We believe that the negative precipitin tests in some cases diagnosed as Hashimoto's disease are mainly due to the lack of sensitivity of the precipitin reaction and not to errors in diagnosis or to heterogeneity within the group. Using the complement-fixation reaction—a more sensitive method for detecting antibody—we obtained positive results in all the untreated cases and in 15 of 16 treated cases of Hashimoto's disease. (The complement-fixation test is relatively non-specific, but in no condition other than untreated Hashimoto's disease has the test been uniformly positive.)

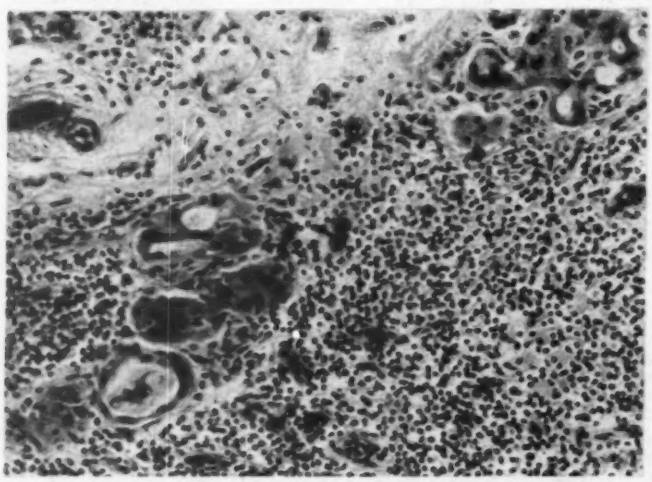

Fig. 2—Thyroid gland in primary myxœdema showing lymphocytic infiltration, fibrosis, and Askanazy cells in surviving thyroid epithelium. (Hæmatoxylin and eosin. ×200.)

The lack of sensitivity of the precipitin test is not surprising, being an inherent feature of this method of detecting antibody. Of greater interest is its apparent lack of specificity : of our 27 positive cases 7 were conditions other than Hashimoto's disease (table I).

In our cases of " simple " non-toxic goitre and malignant disease of the thyroid gland—conditions which may be difficult to distinguish clinically from Hashimoto's disease—the precipitin test has been negative and has not given misleading results, but the number of cases is too small to draw any important conclusions about the value of the negative results in these conditions.

The finding of positive precipitin tests in primary myxœdema (table I) is of considerable interest. It has been suggested that Hashimoto's disease and primary myxœdema are merely different manifestations of the same fundamental disease process (Statland et al. 1951, Skillern et al. 1956). This suggestion conflicts with the views firmly expressed by Joll (1939). The two diseases are similar in the following respects :

(1) They occur predominantly in females of about the same age. In our series the mean age of onset of primary myxœdema (28 cases) was 54 and of Hashimoto's disease (21 cases) 47.

(2) There is hypofunction of the thyroid gland in both.

(3) The erythrocyte-sedimentation rate is raised in both (Luxton and Cooke 1956).

(4) Abnormal serum-flocculation tests are found in both. Skillern et al. (1956) found the colloidal-gold reaction of the serum abnormal in 6 of 11 cases of " primary thyroid failure without goitre," while Luxton and Cooke (1956) found slightly abnormal results in 3 of 14 cases of primary myxœdema.

(5) Thyroid-stimulating hormone does not increase the uptake of $^{131}I$ in either disease (Skillern et al. 1956).

(6) The thyroid gland in primary myxœdema is very like that in Hashimoto's disease. We examined 8 thyroids from patients with primary myxœdema and found in all of them well-developed Askanazy cells (Hürthle cells), infiltration with lymphocytes and sometimes plasma cells, fibrosis, and absence of normal thyroid tissue (fig. 2). These are all prominent features of Hashimoto's disease.

(7) Positive precipitin tests are found almost exclusively in these two conditions (table I).

Hashimoto's disease and primary myxœdema differ in the following respects :

(1) In Hashimoto's disease the gland is enlarged, whereas in primary myxœdema it is small.

(2) Abnormal serum-flocculation tests, a raised serum-γ-globulin level, and anti-thyroid precipitins are found much more often in Hashimoto's disease than in primary myxœdema.

(3) Males are involved more often in primary myxœdema than in Hashimoto's disease. Joll found only 3·7% of males in 81 cases of Hashimoto's disease, and 13·8% of the Clinical Society of London's (1888) 109 cases of myxœdema were in males.

(4) Radio-iodine studies in Hashimoto's disease usually show a normal uptake of $^{131}I$ and normal or high levels of protein-bound $^{131}I$, even in the presence of hypothyroidism (Doniach et al. 1957, confirmed by our own observations), whereas in

primary myxœdema both the uptake of $^{131}I$ and the level of protein-bound $^{131}I$ are low.

In spite of these differences it is difficult to draw a sharp dividing line between Hashimoto's disease and primary myxœdema. For example, 1 of our patients presented with the clinical features of myxœdema, a strongly positive precipitin test, no generalised goitre but a palpable thyroid isthmus, normal flocculation tests, a low thyroid uptake of $^{131}I$, and a 48-hour-protein-bound $^{131}I$ of 0·33% of dose per litre. We cannot diagnose this patient as either Hashimoto's disease or primary myxœdema but regard her condition as being intermediate between the two. In 2 of our cases of untreated Hashimoto's disease (diagnosed because of goitre, abnormal serum-flocculation tests, and raised serum-$\gamma$-globulin) the precipitin test was positive, whereas the $^{131}I$ findings were typical of primary myxœdema. Furthermore, from a study of postmortem thyroids in primary myxœdema and from surgical experience in Hashimoto's disease it is clear that the sizes of the thyroids from patients with these diseases form a continuous series. Our serological findings supply a further link between the two diseases.

We obtained a positive precipitin test in 3 patients presenting a typical clinical picture of thyrotoxicosis (table I). The diagnosis is supported in all 3 by a good response to anti-thyroid therapy and in 2 by typical radio-iodine findings (in the 3rd case the radio-iodine findings are invalid because the patient was receiving thiouracil at the time of testing). In 1 patient the precipitin test was positive before therapy and was accompanied by abnormal serum-flocculation tests. The 2 other patients were tested after treatment: in 1 the flocculation tests were slightly abnormal but were normal when repeated a few days later. In this patient the precipitin test took more than seven days to become positive but when repeated after further radio-iodine therapy it became positive within five days. The 3rd patient, who developed thyrotoxicosis six years ago, became euthyroid on methylthiouracil therapy, which was continued for four years. She now has persistent exophthalmic ophthalmoplegia and a nodular goitre but remains euthyroid without further therapy. In this patient the flocculation tests were normal.

The theoretical implications of the precipitin test in Hashimoto's disease have been recently reviewed (*Lancet* 1957). In 1 case White (1957) has shown, by the fluorescent-antibody technique, that circulating antibody is present which reacts with the patient's own thyroid gland. There is also evidence that the antigenic substance is thyroglobulin, though complete proof of this is lacking because highly purified thyroglobulin has apparently not yet been prepared. Rose and Witebsky (1956) have succeeded in auto-immunising rabbits with an extract prepared from an excised portion of the animals' own thyroid glands, and have demonstrated the development of precipitating thyroid antibody and of pathological changes, said to resemble those of Hashimoto's disease, in the remaining thyroid tissue. These findings suggest that auto-immunisation plays an important part in the ætiology of Hashimoto's disease, in which case it may also be an important ætiological factor in primary myxœdema. If this is so, the differences between the two diseases might be due to differences in the cytotoxicity of the antibodies, in the resistance of the thyroid epithelium to the effects of antibody, or in the original pathological changes (if such exist) in the gland which initiate the auto-immunisation.

We agree with Skillern et al. (1956) that Hashimoto's disease is "compensated thyroid failure" and primary myxœdema "uncompensated thyroid failure." The rather low incidence of antibodies in primary myxœdema may be due to diversity of ætiology in different cases of this disease; on the other hand, it could be attributed to the effect of advanced thyroid atrophy leading to loss of antigenic stimulus and decreased production of antibody. The duration of symptoms in our patients with primary myxœdema tends to support the latter suggestion because, in the 4 cases with a positive precipitin test, the average duration was ten months, whereas in 20 cases with a negative test the average was five years. In this connection it is known that plasma-protein abnormalities in Hashimoto's disease gradually disappear after thyroidectomy or thyroid-hormone therapy (Luxton and Cooke 1956, Doniach and Hudson 1957); and, though it has not been shown that precipitating antibody disappears with treatment, the incidence of positive precipitin tests in treated and untreated cases suggests that this is so.

We have no knowledge of the factors which initiate auto-immunisation. It is conceivable that, even in normal circumstances, antigenic material leaks from the thyroid gland, and that the abnormality is a particular propensity for antibody response. On the other hand, formation or leakage of antigen may take place only in the presence of a thyroid abnormality. Perhaps both factors—an abnormal gland and an unusual ability to form antibodies—are important. In addition to the detection of precipitins in 3 of 123 cases of thyrotoxicosis (table I) we found complement-fixing antibody to thyroid extract in the serum of 62% of 109 cases of thyrotoxicosis, whereas the incidence of such antibody in 419 hospital patients without thyroid disease was only 10·5% (unpublished observations).

In view of these findings it is not unreasonable to suggest that the thyroid-gland abnormality of thyrotoxicosis facilitates the escape of antigenic material. In most of these cases the antibody response is weak, detectable only by the complement-fixation reaction, and apparently does not influence the course of the disease. But in a small proportion of thyrotoxic patients, who are presumably good antibody producers, strong auto-antibodies develop which may be detected by the precipitin test. If we may assume, as seems most likely, that such auto-antibodies have cytotoxic properties, and can bring about in the thyroid gland the changes of Hashimoto's disease, we have a possible explanation of the thyrotoxic features occasionally observed to precede or accompany the onset of Hashimoto's disease (Vaux 1938, Joll 1939, Levitt 1951).

## Summary

With saline extract of thyroid gland as antigen, precipitin tests were performed on the sera of hospital patients with various diseases.

Positive results were obtained in 20 of 32 cases of Hashimoto's disease, 4 of 28 cases of primary myxœdema and 3 of 120 cases of thyrotoxicosis.

Though this is a simple and useful diagnostic test for Hashimoto's disease, probably it is not sufficiently sensitive to supersede serum-flocculation tests and estimation of the serum-$\gamma$-globulin level but should be used in conjunction with them.

The results of the precipitin tests in Hashimoto's disease and in primary myxœdema are compared. They favour the view that at least some examples of both conditions are variants of the same fundamental disease. A possible relation between thyrotoxicosis and Hashimoto's disease is suggested.

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# SHORTENING AND PARALYSIS IN POLIOMYELITIS

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FROM 1945 to 1952 550 children were admitted to Queen Mary's Hospital for Children, Carshalton, with paralytic poliomyelitis. These patients were treated by a method of physiotherapy which has been described in detail by Reynolds (1956). In the acute stage the affected area is treated with hot packs, and gentle passive movements of the joints are performed. During the stage of recovery great emphasis is laid on functional re-education and the stretching of tight structures. Few of the patients wear callipers, and tendon transplantation is rarely undertaken. Although the recovery of useful function in the paralysed leg is often remarkable, the growth of the limb is usually disturbed. The progressive discrepancy in length between the two limbs often becomes the major disability, and in many of the older children equalisation has been attempted by stapling the epiphyseal cartilage of the longer limb. The popularity of this operation has limited the number of adults available for study.

In the present review the fate of those patients who were aged less than 10 years at onset is presented. An attempt was made to contact all the children who had demonstrable lower-limb paralysis at the time of discharge from hospital. At a preliminary analysis those who had recovered full muscle function in the legs and those who had had osteotomies, sympathectomies, or operations on the epiphyseal cartilage were excluded. Each of the remaining patients had a full muscle test. In the lower limb the muscles were examined in twenty groups by the M.R.C. scale, in which 0 represents no contraction and 5 normal muscle power. From this test each limb was allocated a muscle score, the normal limb being recorded as 100. Subtraction of the score of the more paralysed limb from that of its fellow yields the *muscle deficit*.

Measurements of limb length were made from the anterior superior iliac spine to the medial malleolus, and from the anterior superior iliac spine to a sole plate. The total shortening of the leg was then estimated with the patient standing with correcting blocks beneath the shorter limb. The size of each foot was estimated with an instrument which permitted a simultaneous record to be taken of the length and breadth of the foot and of the height of the upper aspect of the talus from the floor. Throughout this paper the length of the limb is derived from the measurements from the anterior superior spine to the medial malleolus. Using the height of the arch as a correcting factor it is possible to check this figure against the total length of the limb recorded by the other two methods. Difficulties were occasionally experienced in the presence of deformity and of obesity and when the patient could only stand with difficulty. Where the three observations did not agree within the limit of 0·5 cm. the patient was excluded from this series.

The girth of each thigh was recorded at its mid-point, and the greatest diameter of each calf was also measured. The wasting of thigh and calf was calculated by subtraction of the circumference of the more wasted limb from that of its fellow. The wasting of thigh and calf was expressed as a percentage of the circumference of the better limb, and the mean of these two percentages was used as an *index of wasting*. Amongst the other data recorded only the persistent use of a calliper will be discussed here.

The number of patients with residual leg weakness who attended for examination was 144. Of these, 20 were fully grown and will only be briefly considered. There were 19 patients whose measurements were deemed inaccurate on the criteria given, and these have been excluded. Of the rest, 50 had a bilateral lower-limb paralysis and 55 had no detectable muscle loss in one leg but a variable amount of paralysis in the other. To compare the disturbance of growth in these patients, none of whom was yet mature, the total shortening was divided by the number of years since the onset of paralysis. The result is the *annual shortening*, and this figure, rather than the total shortening, was used in the analysis of the data. In using this term it must be remembered that the actual growth, even of a completely paralysed limb, is usually within 80% of the normal. It is, however, the difference between the two limbs which is of clinical importance.

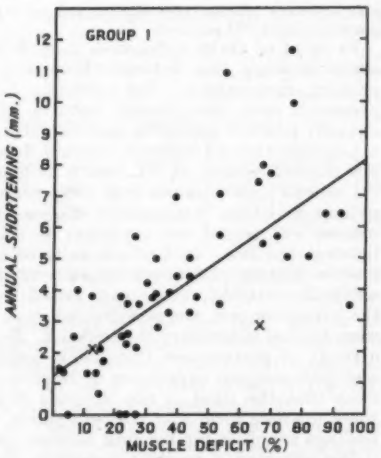


Fig. 1—Correlation between annual shortening and muscle deficit of 55 patients with residual paralysis of one leg only ($r=0{\cdot}64$): x, two observations.

## Unilateral Paralysis

The annual shortening, the muscle deficit, and the index of wasting of the 55 patients with a residual unilateral paralysis were as follows:

| | *Annual Shortening* (mm.) | *Muscle Deficit* (%) | *Wasting* (%) |
|---|---|---|---|
| Mean .. | 4·0 | 39·3 | 16·2 |
| Standard error | ±0·35 | ±3·4 | ±1·3 |

The individual observations are shown in fig. 1. It can be seen that shortening increases progressively with the loss of muscle power, but the range of the observations is considerable. 4 patients have obvious muscle weakness without shortening, and 3 others, who were not the most severely paralysed, showed an increase in shortening of 10 mm. or more a year. The correlation coefficient is 0·64, which suggests that the association between shortening and paralysis is significant. The regression coefficient is 0·07; hence an increase in the muscle deficit of 10 might be expected to yield an increase of 0·7 mm. in the annual shortening.

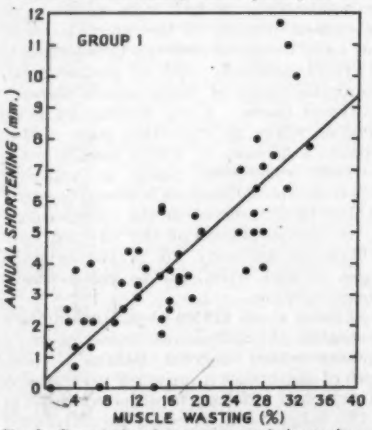


Fig. 2—Correlation between annual shortening and muscle wasting of 53 patients with residual paralysis of one leg only ($r=0{\cdot}86$).

A similar diagram can be constructed for the relationship between shortening and muscle wasting (fig. 2). Observations on 2 patients are not avail-

able, and the figure therefore includes only 53 patients. There are 3 patients without shortening who are wasted, and there are still 3 patients whose shortening appears out of proportion to the wasting. The observations as a whole, however, are less scattered than those in the first group, and the coefficient of correlation improves to 0·86.

### Bilateral Paralysis

The difficulties in the analysis of the patients with bilateral residual weakness lie largely in the absence of a suitable control. In many of these patients the growth of both legs is apparently affected, and the ratio between leg length and trunk appears to be disturbed. It was initially felt that simple measurements of the standing and sitting height in this group would permit deductions to be made about the shortening of both limbs, but the method has too great an error. These patients often have an associated trunk weakness which influences the sitting height substantially.

If the patients with a residual bilateral weakness follow the same pattern as those with a unilateral disturbance, one would certainly expect each leg to be short, and the difference between the two to be related to the difference in muscle power in the two limbs. In fact, throughout this series, the more paralysed leg was always the shorter. When the muscle score of the weaker leg is subtracted from that of the stronger, a mathematical expression of the muscle difference is obtained. The average difference of muscle power, and the average shortening, is very similar to that of the patients with unilateral paralysis:

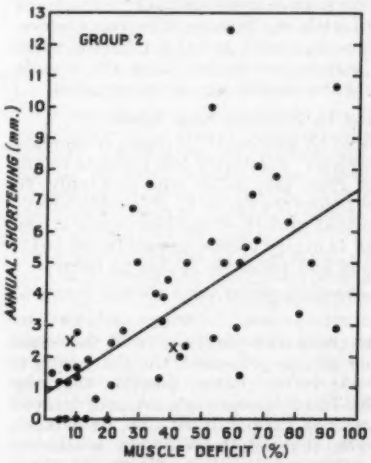


Fig. 3—Correlation between annual shortening and relative muscle deficit of 50 patients with bilateral residual paralysis (r=0·6).

| | *Annual Shortening* (*mm.*) | *Muscle Deficit* (%) | *Wasting* (%) |
|---|---|---|---|
| Mean .. .. | 3·65 | 38·5 | 12·3 |
| Standard error | ±0·41 | ±3·7 | ±1·2 |

In fig. 3 the annual shortening has been plotted against the difference in muscle power. It can be seen that the observations vary widely, but there is again an increase in shortening with an increasing difference between the legs. There are 3 patients with an annual deficit of 10 mm. or more, and again these are not the patients in whom the difference of muscle power is the greatest. If wasting is used as an index of muscle loss (fig. 4), the scatter of the observations is slightly less, and the coefficient of correlation is improved from 0·6 to 0·66.

### Influence of Individual Muscle on Limb Length

It is commonly stated that certain muscles are more important than others in the maintenance of limb length, and paralysis of the calf is often said to be associated with severe shortening. Strict proof of this statement demands the examination of patients with paralysis of a single muscle group; and, with the exception of the foot invertors, paralysis of this type is extremely uncommon. In the patient with scattered muscle weakness the influence of single muscles may be masked by the associated pattern of paralysis. Nevertheless, if the shortening associated with the varying strengths of individual muscles is recorded, the resulting analysis should indicate whether one or more muscle groups are of supreme importance in the production of shortening. The method may fail where a muscle is frequently paralysed in isolation, that is, its influence may be hidden by the strength of other muscles.

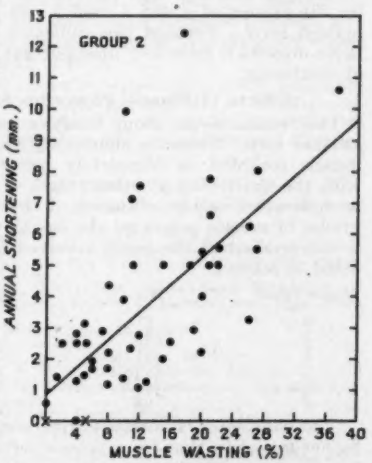


Fig. 4—Correlation between annual shortening and relative muscle wasting of 50 patients with bilateral residual paralysis (r=0·66).

The analysis which is presented in fig. 5 is derived from the 55 patients with unilateral paralysis. For simplicity the muscles are considered in twelve main groups; and, where two muscles have been grouped together, the mean of their strengths has been recorded. The annual shortening associated with various muscle powers of each of the twelve groups has then been charted. Thus, when the power—e.g., of the gluteus maximus muscle—has been determined, the annual shortening of the limb has been recorded against this power, the associated muscle disturbance being ignored. The mean of the values has then been recorded in the form of a histogram.

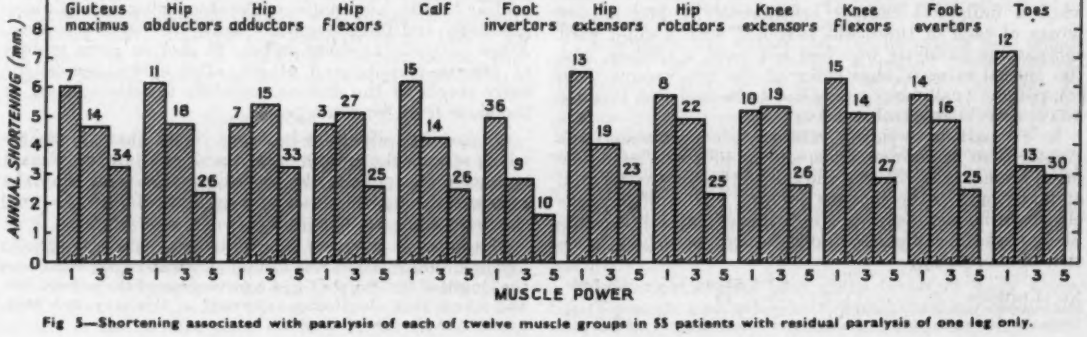


Fig 5—Shortening associated with paralysis of each of twelve muscle groups in 55 patients with residual paralysis of one leg only.

Most of the muscle groups in fig. 5 show an association between the severity of their involvement and the amount of shortening of the limb: and, although this is greater for the muscle of the toes than for other groups, the difference is not statistically significant. The hip flexors, hip adductors, and knee extensors, muscles which Sharrard (1955a) has shown to have an associated pattern of paralysis, exhibit a rather different histogram from the others. For these muscles shortening is maximal in the middle ranges of muscle power. The difference between these three muscle groups and the other nine is significant for the powers of 0 and 1, and 2 and 3, but not at the highest level. Perhaps this indicates that paralysis of these muscles is relatively unimportant in the production of shortening.

### Effects of Muscle Power on Shortening

The results of the group analysis can also be used in another way. When the shortening associated with each muscle recorded as completely paralysed is compared with the shortening at other stages of the M.R.C. scale, an indication can be obtained of the effects of varying grades of muscle power on the length of the limb. This is independent of the group involved and is briefly indicated as follows:

| *Muscle Power* | *No.* | *Mean Annual Shortening (mm.)* |
|---|---|---|
| 0 | 87 | 5·7 ±0·24 |
| 1 | 61 | 5·88 ±0·33 |
| 2 | 57 | 5·22 ±0·32 |
| 3 | 145 | 4·47 ±0·22 |
| 4 | 143 | 3·2 ±0·29 |
| 4+ | 74 | 2·64 ±0·18 |
| 5 | 93 | 2·0 ±0·14 |

The shortening associated with complete paralysis is rather less than that for a muscle power of 1 but rather greater than that at the power of 2. These differences are slight, however, and without statistical significance. Further increases of muscle power are associated with a steady diminution of shortening, and the relationship between muscle power and shortening is roughly linear. When this is expressed graphically (fig. 6), the importance of Sharrard's (1955b) suggestion of 4+ as a distinct stage in muscle recovery becomes apparent. It therefore appears that variations in power of muscle below the level of contraction against gravity have little influence on the length of the limb.

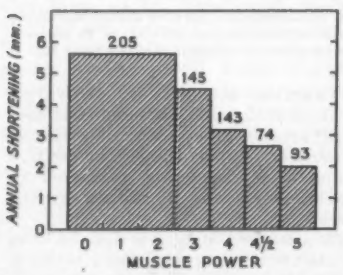


**Fig 6—Effect of muscle strength, independent of group, in production of limb shortening in 55 patients with residual paralysis one leg only.**

### Effect of Calliper on Shortening

Over the whole series there were 24 patients who had worn a unilateral calliper continuously. The muscle power of each of these was matched with a child with comparable paralysis who had not worn a calliper, and the annual rates of shortening of the two groups were compared. 2 calliper patients had to be excluded because no comparable control was available.

In 12 patients wearing callipers the shortening was greater than in their controls, and in 10 it was less. The mean annual shortening of the calliper group was 5·4 mm. annually, and of the controls 5·5 mm. This difference is clearly of no significance. From this evidence it appears likely that the calliper has no influence upon the production of shortening.

| | *Calliper* | *Controls* |
|---|---|---|
| No. of patients | 22 | 22 |
| Mean muscle deficit (± s.e.m.) | 60 ±1·9 | 58·7 ±1·59 |
| Mean shortening in mm. (±s.e.m.) | 5·4 ±0·54 | 5·5 ±0·62 |

### Tightness

Most patients with a residual paralysis also present with a detectable shortening of myofascial structures, and this shortening may be apparent very early in the course of the disease. In the production of contractures muscle imbalance plays an important part, and this is certainly true of the present series, but the clinical picture is also clearly affected by the efficiency of treatment. The main deformities in the leg are associated with shortening of the plantar fascia, calf muscles, hamstrings, hip flexors, and tensor fasciæ latæ, and the tightness of each of these structures has been estimated clinically and classified either as slight, moderate, or severe.

There is no doubt that patients with limbs which are little disturbed in their growth also show little in the way of contractures, and that severe shortening is often associated with severe deformities. There are, however, many exceptions to this rule, and there is no evidence that muscle contractures alone play an important part in the production of shortening. Patients with contractures with slight muscle weakness show little disturbance of growth, whereas severe weakness without contractures is usually associated with shortening. The two factors, muscle loss and tightness, usually go hand in hand; when they diverge, the muscle loss rather than the muscle contracture indicates the shortening to be expected.

### Shortening in Patients Now Adult

Shortening produced by poliomyelitis ceases to increase when growth is complete. Relatively few patients retain an untreated short limb into adult life, and only 20 adults with an onset before the age of 12 years were examined. If we assume that growth of the legs ceases at the age of 16 in boys, and 14 in girls (Green and Anderson 1947) the annual shortening and paralysis appear as follows:

| | *Annual Shortening (mm.)* | *Muscle Deficit (%)* |
|---|---|---|
| Mean | 2·8 | 37 |
| Standard error | ±1·0 | ±6·2 |

Although in this group the paralysis is of the same order as in the other groups presented, the shortening is considerably less. It is, of course, possible that the shortening diminishes in adolescence as a result of delayed fusion of the epiphysis on the paralysed side. It is much more likely, however, that adults represent a selected series and contain a larger proportion of patients whose shortening was too slight to consider surgical correction. Many of the others have already had operative correction for the shortening extremity and therefore fall outside the series.

### Shortening and Age of Onset

In any analysis of shortening in poliomyelitis it is important to consider the progress of the discrepancy between the limbs as age advances. In the present paper the total shortening has been reduced to a figure which expresses the annual increase in shortening, and it is assumed that this figure is a fairly constant indication of the depression of growth. Although detailed studies of the growth of the paralysed limb are not available, it is clear that in most patients the shortening does increase gradually and fairly regularly until growth is complete. A few patients, however, appear to shorten more rapidly at certain periods, and others, after shortening in the early stages of the disease, maintain the discrepancy at the same level for some years.

On general principles it seems likely that the factor which retards the growth of the paralysed limb will remain operative throughout the growing-period, and that the younger the age of onset the greater will be the final shortening.

Stinchfield et al. (1949) studied 64 patients with unilateral leg involvement before the age of 11 years. They expressed the length of the shorter leg as a percentage of the normal one, and found that shortening expressed in this way was independent of the age of onset.

Gullickson et al. (1950), using the same method but apparently including children who were still immature at the time of examination, reached similar conclusions, although their figures suggest that the younger the onset the greater will be the shortening. Nevertheless, unless the onset is after the age of 10 years, this difference is very small.

The implications of these two papers appear to be that the effect of paralysis on growth increases as age advances, and that this effect is maximal about the age of 10 years and then rapidly diminishes.

In the Carshalton series it has been impossible to elucidate the effect of age upon onset partly because the number of adults studied was small and partly because these adults appeared to represent a selected group in whom correction of the leg discrepancy was either unnecessary or undesirable. In the children examined not only the total shortening but also the annual shortening was greater in those with an onset in infancy. However, the early onset was also associated with a more severe paralysis, and the further analysis of the age factor was therefore abandoned.

### Cause of Shortening of Limb

The demonstration of an association between shortening and paralysis does not, of course, indicate cause and effect. Indeed it is difficult to understand why any muscular disturbance should influence the growth in length. Certainly muscle pull influences the diameter of a bone, both in the child and in the adult, and in the laboratory animal. Stimulation of osteogenesis in these circumstances probably results from direct traction on the periosteum. Growth in length, however, depends on the epiphyseal cartilage, an area which is relatively uninfluenced by mechanical factors.

The demonstration by Haas (1945, 1948) and by Blount and Clark (1949) that epiphyseal growth can be prevented or restrained by inserting staples across the epiphyseal cartilage has suggested that shortening in poliomyelitis might be due to the longitudinal restraint of fibrotic muscles; but Strobino et al. (1952) have shown that epiphyseal growth cannot be restrained by a pressure of 60 lb. per sq. in., and Blount and Zeier (1952) have also commented on the very high pressure which develops within the epiphyseal cartilage after stapling. It seems most unlikely that contractures of muscle can exert such high forces evenly over the epiphyseal cartilage, although they may produce local areas of pressure which encourage angular deformities.

In the absence of any obvious mechanical cause for the shortening after poliomyelitis attention has turned to the vascular changes which take place in the legs. There can be little doubt that the paralysed limb, which is cold and often blue, has a lower resting blood-flow than its fellow. Whether in addition there is an associated autonomic disturbance, either peripherally (Goetz et al. 1955) or centrally (McPherson and Kessel 1955) remains to be proved. In either case it is unlikely that an autonomic derangement is the major factor in the production of shortening, since the overgrowth of bone which can be produced by sympathectomy is very slight (Harris and McDonald 1936, Robertson 1934, Barr et al. 1950). If the failure of growth is due to a vascular factor, this must be caused mainly by the loss of muscle power and substance.

### Conclusions

Limb shortening in poliomyelitis is related directly to the extent of the paralysis and the loss of muscle bulk. When the paralysis is bilateral, the shortening of the more paralysed limb is in proportion to the difference between the muscle power of the two limbs. Variations between individual patients are too great, however, to permit this to be used to predict the final discrepancy in limb length.

With the exception of the hip flexors, hip adductors, and knee extensors, which appear to be relatively unimportant in the maintenance of limb length, there is no evidence that paralysis of any single muscle group plays a major part in the production of shortening. Whether a muscle is completely paralysed or is just capable of contraction is unimportant, but recovery of contraction against gravity, or recovery to each of the higher levels of muscle power, is associated with a lower level of annual shortening. There is no evidence that the use of a calliper or the presence of myofascial contractures significantly affects the amount of shortening.

It is unlikely that the influence of muscle paralysis on bone growth is a mechanical one, but the association between paralysis and shortening suggests that the loss of muscle bulk may induce a vascular insufficiency which influences the growth of bone.

It is a pleasure to record my appreciation of the assistance afforded to me by Dr. David Lawson, Mr. R. H. Metcalfe, Miss M. M. C. Reardon, Mr. R. J. S. Reynolds, and Miss M. Messenger of the poliomyelitis unit at Queen Mary's Hospital for Children, Carshalton.

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## ACUTE CHLORPROMAZINE POISONING

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A CASE of acute chlorpromazine poisoning is here recorded to emphasise the danger of massive doses and to report a dramatic initial response to treatment.

A woman, aged 46, had had multiple sclerosis for eight years. The disease involved mainly the legs, and stiffness and difficulty in walking had gradually progressed till the legs became fixed in flexion. The day before admission, pain (due to flexor spasms) became unbearable, and her general practitioner prescribed a hundred 25-mg. tablets of chlorpromazine. She swallowed all the tablets (2500 mg.) at 3 A.M. and at 7 A.M. her husband was unable to rouse her. She was admitted as an emergency. She did not, at any time, vomit or become jaundiced.

She was in deep coma, and painful stimulation evoked no response. The blood-pressure was unrecordable. The respiratory-rate was 4 per min. The pupils were small and reacted extremely sluggishly to light. The upper limbs were flaccid and the deep reflexes absent. The lower limbs were fixed in flexion, the knees close to the chest wall.

The stomach was washed out, but no tablets were found. Analysis of the aspirate showed 52 mg. of chlorpromazine. She was then given 10 mg. of nalorphine intravenously. In less than ten minutes the respiratory rate rose to 20 per min. and the depth of respiration improved dramatically. The blood-pressure was recordable (50/45 mm. Hg, and ten minutes later 100/60). The coma became lighter and there was some return of the deep reflexes in the limbs. At no time had she been given morphine, pethidine, or methadone.

Next day she regained consciousness but remained rather drowsy. Her temperature never fell below 97°F. She died of widespread bronchopneumonia during her seventh day in hospital.

Chlorpromazine has been given in larger daily doses than the single dose taken here, particularly in psychiatric practice (Kinross-Wright 1955); but these large amounts

are always given in divided doses, gradually increased to maximum dosage over several days. Recovery from chlorpromazine poisoning has been reported by Aubertin et al. (1954), Vallat and Lepetit (1954), Hopkin (1955), Fontan et al. (1955), and Langeron et al. (1955).

In man, nalorphine initially stimulates respiration, counteracting the depression caused by pethidine, methadone, and morphine; but this effect, though dramatic, is brief, and may result in after-depression, since nalorphine reduces the sensitivity of the respiratory centre to carbon dioxide by 50%. It has no significant wakening effect. There seems little doubt that in the case recorded here nalorphine dramatically increased the respiratory rate from 4 a minute to 20 a minute in a very few minutes. The patient's cyanosis disappeared, and the blood-pressure became recordable.

I have seen another case of chlorpromazine poisoning in which respiratory depression responded dramatically to nalorphine; this will be reported elsewhere.

SUMMARY

A case is reported of acute chlorpromazine poisoning in a woman with multiple sclerosis. Severe hypotension and respiratory depression responded to intravenous nalorphine. The patient later died of bronchopneumonia.

I am indebted to Dr. W. R. Gauld for kind help and permission to publish this case.

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# CEREBRAL ŒDEMA

## FOLLOW-ON TREATMENT AFTER CARDIAC RESUSCITATION AND RESPIRATORY CRISIS

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THE practice of resuscitation after cardiac arrest or ventricular fibrillation is continually expanding (Stephenson et al. 1954, Johnson and Kirby 1954, Cole and Corday 1956, Milstein 1956). It seems appropriate to endorse the importance of starting cerebral dehydration therapy (Seldon et al. 1949, Lucas 1950, Cole 1951, Sadove et al. 1953, Argent and Cope 1956) as soon as possible after restoration of normal heart rhythm, or after any acute hypoxic episode. Experience gained in the following two cases emphasises this point. The successful outcome of the first case supports the view that it is the cerebral œdema following an acute anoxic episode which is responsible for permanent cerebral damage or even death.

### Case-reports

**Case 1.**—A man, aged 22, not in cardiac failure, underwent mitral valvotomy on Jan. 3, 1957, under general anæsthesia. Commissurotomy was successful, the operation was uneventful, and the patient left the theatre in good colour, breathing spontaneously, and partially conscious, with an airway in position. He reached the ward cyanosed, with shallow breathing, and gasping. Medical attention was sought, but before it could be obtained respiration ceased and no pulse could be felt. Manual artificial respiration and attempts to inflate the lungs with the B.L.B. mask and reservoir bag were useless. An endotracheal tube was passed and positive-pressure oxygen inflation begun. It seemed clear that the heart had stopped for so long that further resuscitation was useless. Later it was calculated critically that the heart had stopped for at least $5^1/_2$–6 minutes after a period of hypoxia possibly lasting minutes.

*Cardiac Massage.*—Nevertheless the operation wound was rapidly reopened and the heart was found arrested, cyanosed, and turgid. Cardiac massage restored the beat after 30 seconds, the rate being 140 a minute, and the rhythm regular. 2 ml. of adrenaline 1/10,000 solution was injected into the left ventricle during initial massage. Fifteen minutes later the wound was resutured in the theatre, and the left pleural cavity drained to an underwater seal. Continuous oxygen inflation had been maintained, but spontaneous respiration was adequate by the time the wound was closed. The patient was gradually weaned to air during the next half-hour, the endotracheal tube remaining in position.

*Cerebral Œdema.*—At this point the development of cerebral œdema was considered, and 25 ml. of 50% glucose was injected intravenously. This dosage was repeated about hourly for the next five hours. Slow but steady improvement took place, respiratory excursion being much increased. Initial muscle flaccidity was superseded first by upper-limb spasticity and then by good muscle tone in all the limbs. On several occasions a cessation of improvement, with increasing unconsciousness, was noted about 50 minutes after the injection of glucose. This was regarded as an indication for further glucose, after which improvement was resumed. During this period pyrexia developed and was treated by cool sponging, with good result.

*Tracheotomy.*—In view of the likelihood of prolonged unconsciousness, and the bronchial secretions already being obtained, tracheotomy was carried out six hours after the cardiac arrest. A cuffed tracheotomy tube was used so that inflation could be effected in case of respiratory distress. A Ryle's tube was passed in anticipation of feeding during unconsciousness but was not used. The pulse-rate fell to 80.

*Treatment in Ward.*—The patient returned to the ward with oxygen administered into his trachea through a catheter. He was immediately placed in a sitting position and improved dramatically at once. Return to partial consciousness was almost sudden; his eyes opened, and his head turned towards a calling voice. Intravenous dextrose 5% was slowly given, and 25 ml. of 50% glucose was given intravenously about every $1^1/_2$ hours during the remaining ten hours of the night. Two further doses of 50% glucose were given next day. Bronchial suction was applied at short intervals during the night, and full consciousness slowly returned. In the morning, seventeen hours after the cardiac arrest, the patient was conscious, drowsy, and confused, but obeyed commands, and moved and coughed well. Catheterisation of the bladder was necessary. Twenty-four hours later recovery seemed complete. The pleural drain was removed, and the tracheotomy tube was taken out on the second postoperative day. Voluntary micturition was established.

*Further Progress.*—The patient had almost no retrospective amnesia, but mild confusion about current incidents was present during the first four days. At later dates preoperative amnesia appeared to be about three hours, and his memory and intelligence were considered to be normal by the staff and by his relations. Neurological examination was normal. Acute pericarditis developed on the sixteenth day, but aspirated pericardial fluid was sterile on culture, and the condition subsided in ten days on chemotherapy. The cardiac failure associated with his pericarditis delayed recovery, but he was discharged home ten weeks after the operation.

**Case 2.**—A man, aged 57, with an extensive syphilitic aneurysm of the aortic arch was submitted to general anæsthesia on May 22, 1957, for aortography by percutaneous arterial puncture. He was orthopnœic and mildly cyanosed and had a typical brassy cough with associated bronchiolitis. Previous attempts at aortography had shown that, after the administration of relaxants, pulmonary inflation could only be achieved when the patient was placed sitting up. On this occasion, therefore, anæsthesia was maintained in this position and inflation continued until good respirations were present. About half an hour later respiratory distress, due to bronchial secretions which could not be coughed out, developed; rapid loss of consciousness and deterioration took place. An endotracheal tube was again passed, the bronchi were frequently aspirated, and the lungs were inflated with oxygen. Peripheral circulatory failure was severe, intravenous methedrine 15 mg. was given, and a bottle of concentrated plasma was infused. Because of the acute-on-chronic hypoxia 50 ml. of 50% sucrose was given intravenously. Within a few minutes partial consciousness and good spontaneous respiration returned. No regressive tendency was noted in this case, and a second dose of sucrose was not necessary for three hours. Once again

improvement was rapid. Two further injections of 50% sucrose were given at six-hour intervals. Consciousness was steadily regained, and the patient reached his preoperative condition twelve hours after the incident.

### Discussion

The value of anticipating and treating cerebral œdema following hypoxia was shown clearly by the impressive changes following dehydration therapy.

The use of glucose in case 1 was occasioned by circumstance rather than choice; thereafter sucrose was stored in theatre and ward. Bullock et al. (1935) and Gregersen and Wright (1935) have shown experimentally that sucrose is preferable because it does not produce the secondary rise in pressure of the cerebrospinal fluid (C.S.F.) as does glucose. In addition, up to 50% of the glucose given may be stored in body tissues, reducing its dehydration value in the brain, and may cause tissue œdema if water is given later. The "rebound phenomenon" of glucose was clearly seen in case 1. Feher et al. (1942) suggested that sucrose should not be used in renal and cardiac diseases; the evidence is limited. Ellis and Faulkner (1939) show that the hæmodynamic strain effects of the two substances are identical. Argent and Cope (1956) discuss the relative effects of sucrose, glucose, sodium chloride, concentrated plasma, and dextran in detail.

It is the practice at this hospital to make free use of tracheotomy in many instances of prolonged unconsciousness, respiratory failure, and postoperative infection. Sadove et al. (1953) also recommend this but comment on the difficulty of inserting a cuffed tube. They prefer an uncuffed tube, with high pressure ventilation which also ejects pharyngeal secretion. We had no difficulty in using a cuffed tube.

Tracheotomy enabled the patient to be nursed sitting up while unconscious, and remarkable improvement followed the adoption of this posture. Probably the lowering of hydrostatic pressure in the C.S.F. thus achieved further aids cerebral dehydration. In this we differ from Sadove et al. (1953), who recommend a head-down position. The sitting position can be used even in minor degrees of vasomotor collapse if vasopressor drugs are given, since, as Schmidt (1950) pointed out, the cerebral vessels are virtually insensitive to drugs which constrict other blood-vessels. This technique was adopted of necessity in case 2.

Case 1 is of particular interest because of the complete recovery after cardiac arrest in excess of the four-minute limit (Cole and Corday 1956). Johnson and Kirby (1954) point out that this 4-minute maximum may be significantly shortened if hypoxia has existed for any length of time before cardiac arrest occurs.

### Summary

Cerebral dehydration is described in 2 cases of hypoxia. Sucrose is preferred to glucose.

The survival of a patient who had cardiac arrest for about six minutes is described.

The value of tracheotomy and position is emphasised.

I wish to thank Mr. J. Leigh Collis, who performed the mitral valvotomy, and Mr. R. Abbey Smith, for permission to report their cases. Dr. G. A. Rawlins initiated dehydration therapy in the first case, and to him and Dr. D. R. Rigg I am especially grateful for very valuable assistance as the anæsthetists concerned. The care and observation of our nurses were significant factors in the recovery of these patients.

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## Preliminary Communication

# THE TREATMENT OF METAL POISONING WITH PENICILLAMINE

THE chelating agent penicillamine (β, β-dimethylcysteine) was first introduced as a treatment for Wilson's disease (hepatolenticular degeneration) by Walshe [1] and its use is now widespread. It appears to be more efficacious than dimercaprol (BAL) and edathamil calcium-disodium (calcium versenate) and is effective when given by mouth. High dosages may apparently be given for a long period with safety. We report here its use in two cases of lead poisoning, one of hæmosiderosis, and one of hæmochromatosis.

*Lead Poisoning*

CASE 1.—A worker in a lead smelter was found to have a greater number of stippled red blood-cells per high-power field than is considered consistent with safety and was subsequently removed from the exposure area. His urinary lead was 510 μg. per litre; after two days' treatment with penicillamine 0·3 g. t.i.d. half an hour before food his urinary lead was over 2000 μg. per litre. About this time he became free from symptoms, but since they were mild and would have been expected to disappear nothing positive can be said about them.

CASE 2.—A woman worker who had been intermittently exposed to lead vapour for several years was admitted to hospital with severe abdominal colic, anæmia, and symptoms suggesting peripheral neuritis. After a month's conventional treatment of lead poisoning no clinical improvement was noted. Penicillamine 0·3 g. t.i.d. half an hour before food was then given for fourteen days. The urinary lead before this treatment was 530 μg. per litre; after four days' treatment it was 1530 μg. per litre; and after thirteen days' treatment it was over 2000 μg. per litre. At this time the patient began to show a steady and striking remission of symptoms and was soon completely relieved.

*Hæmosiderosis*

CASE 3.—A man with aplastic anæmia had had several hundred blood-transfusions and as a result acquired liver disease and other signs of iron intoxication. His urinary excretion of iron was 2·8 mg. in twenty-four hours. He was given penicillamine 0·3 g. t.i.d. half an hour before food for three days. On the second day his urinary iron was 2·5 mg. in twenty-four hours, and on the third day 5·5 mg.

*Hæmochromatosis*

CASE 4.—A woman with hæmochromatosis showing bronze diabetes was given penicillamine 0·3 g. t.i.d. half an hour before food for twelve days. Her twenty-four-hour urinary iron excretion was determined daily and there was no significant change during the experiment.

This evidence suggests that penicillamine may be of use in the therapy of metal intoxications other than hepatolenticular degeneration. Further investigations are warranted because of its apparent ability to produce a rapid diuresis of copper, lead, and iron in poisoning with these metals.

We wish to thank Dr. A. G. Richards and Dr. R. E. Beck for their cooperation in this study, and Dr. C. N. Brown, of the Distillers Company (Biochemicals) Limited, for the penicillamine.

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# Medical Societies

## BRITISH ORTHOPÆDIC ASSOCIATION

The autumn meeting was held in London on Oct. 3–5, under the presidency of Mr. PHILIP WILES.

### Genetics in Orthopædics

Dr. CEDRIC CARTER (London) said that orthopædic conditions could be divided into three groups: (1) those where an abnormal genetic constitution, often a single gene mutation, was solely responsible; (2) those due purely to environment; and (3) those, such as congenital dislocation of the hip, where both factors were significant. Studies of monozygous twins had proved most helpful in differentiating these groups, group 1 being always concordantly affected, group 2 being no more often concordant than dizygous pairs, and group 3 showing notably greater concordance than in dizygous pairs (e.g., in congenital talipes equino-varus there was a 23% concordance in monozygous twins but only 2% in dizygous twins). Environmental diseases were becoming less common with improved public health, while largely genetic ones tended to become more common, not only with the increase in mutations due to radiation, but also because better medicine had led to a greater survival and therefore reproductive rate amongst those possessing such mutants. Herein lay a danger unless it was counteracted by advice to such parents on the risks to their children.

Dominant mutations produced an effect even in heterozygotes (i.e., when the mutant gene was paired with a normal gene on the other chromosome of the pair); but the recessive produced an effect only in homozygotes (i.e., paired with another of similar type). Family histories showed that achondroplasia and dysplasia epiphysialis multiplex were the result of dominant mutant genes, whereas Morquio's form of osteochondrodystrophy was usually dependent on a recessive mutant gene.

With dominant genes a family prognosis was straightforward; sporadic cases would be due to fresh mutations, and later brothers and sisters were most unlikely to be affected. But the risk for the children of those affected, if they survived into adult life and married, would be 50%. With recessive mutations, once an affected child had been born the risk for later children was 1 in 4, but the normal brothers and sisters and the affected child, if surviving, would not have affected children unless they were unlucky enough to marry a carrier. The main hope for prevention here lay in finding ways of detecting clinically normal heterozygotes, and warning them of the risks to their children if they marry each other. This was now being done in Italy, for example, to reduce the prevalence of Cooley's anæmia.

A special class of recessive mutations was that of the X chromosomes, where heterozygous females having two X chromosomes were clinically normal, but males with the mutation on their single X chromosomes were not protected by a normal gene on the Y chromosome and were affected. Most childhood muscular dystrophies were due to sex-linked recessive mutations. This was true of all those who were severely affected and were off their feet by the age of 11 years. They were all boys, and their families showed a sex-linked recessive pattern of inheritance. The milder, but otherwise similar, cases were as common in boys as in girls and were mostly due to an ordinary, not sex-linked, recessive mutant gene.

In congenital dislocation of the hip, 6–7% of the sisters of affected children were also affected, and about the same proportion of daughters. Brothers and sons were less often affected. This might be due to a dominant mutant gene with only a 5th to a 10th of the females with the gene clinically affected, and even fewer boys with the gene affected. The environmental factors concerned were not fully known. The condition was commoner after breech birth, and Record and Edwards had recently shown that it was also commoner in the first-born and in babies born in winter. Before we could hope to reduce the incidence of such affections much further work was needed to pick out those with the genetic constitution for the disorder but clinically unaffected, and the environmental factors which lead to the clinical manifestation of the genetic constitution.

### Diaphyso-epiphysial Resection for Tumours of Knee

Prof. MERLE D'AUBIGNÉ (Paris) recommended that this procedure be considered for certain giant-cell tumours, or in suitable cases of sarcoma when amputation was refused. Acrylic prostheses to bridge the gap tended to loosen and break, and massive homogenous grafts were slow to unite and all underwent aseptic necrosis. Autogenous grafts were better, but had proved very liable to fracture. He now recommended the use of a very long Küntscher nail to maintain length and rigidity, with a massive autogenous graft consisting of the anterior half of the upper two-thirds of the tibia rotated through 180° so that the lower end fitted a notch cut in the remains of the femur. The posterior part of the gap and the space left in the front of the tibia were filled with grafts from the bone-bank. His first 9 cases had given encouraging results.

### Sequestrectomy in Chronic Osteomyelitis

Mr. ARTHUR BRYSON (Kano, Nigeria) said that gross chronic osteomyelitis with honey-combed involucrum and massive sequestrum was still common in undeveloped countries. To leave the area packed open after sequestrectomy, as in the Winnett-Orr method, led to very slow healing with excessive scar-tissue formation, thin skin cover of poor quality, and considerable risk of recurrence. After sequestrectomy and full saucerisation of the involucrum, he preferred to suture the skin lightly over a dry gauze pack and suitable antibiotics, and to perform delayed primary suture four to six days later. He did not recommend relaxing incisions—the blood-supply to the skin was too poor in these very chronic cases—but occasionally a pedicle flap was helpful. He had found muscle flaps useless for filling the dead space left by this method. The cavity filled naturally with blood-clot, which was harmless as long as it did not raise the skin-flaps. Streptomycin and penicillin were injected into the cavity on alternate days for a week; the hæmatoma occasionally needed aspiration. Complete healing was obtained very early by this method; a few scars broke down centrally on a small scale, but the small area of bone thus exposed soon healed over.

### Histological Structure of Bone

Prof. D. H. COLLINS (Sheffield) said that in the first stage of development of membrane bone there was proliferating mesenchymal tissue that came under the influence of ill-understood osteogenic factors; they might be the products of certain epithelial cells. Then followed the production first of argyrophil reticulin fibres, and then of collagen fibres by the fibroblasts, together with a mucopolysaccharide base substance. The resultant tangle of fibres (the woven bone anlage) enmeshed cells which became osteocytes and formed a calcifiable medium in which the primitive bone islands developed. Around these islands osteoblasts appeared laying down lamellæ of osteoid tissue with parallel-running fibres. Lamellar bone differentiated from this tissue and was eventually substituted for all the woven bone, which was removed by osteoclasts as the marrow spaces and their contained tissues developed. In mature lamellar bone the osteocytes had long processes all interconnected, and he mentioned the importance of the endosteal osteoblasts, the endosteum being far more extensive than the periosteum. The exact mechanism of bone resorption by the osteoclasts was still unknown.

### Mechanical Properties of Bone

Prof. G. H. BELL (Dundee) discussed experiments designed to measure the strength and elasticity of bone. In long bones the effects of twisting, compression, and traction were difficult to measure, while investigations of bending stresses were relatively easy to devise and measure experimentally. His figures showed that bone was of a strength comparable to that of cast iron, although stress-strain graphs showed a very different pattern. In rats a low-calcium diet resulted in more fragile bones, but the actual breaking stress remained constant per unit of material in cross-section—i.e., the quality of the material remained unaltered, as also in limbs to which the anterior nerve-roots had been divided. In contrast to this, in lathyrism, which was a condition of collagen poisoning, the breaking stress was reduced by 25% though bone weight and ash content remained unaltered. It was not known whether this was due to alterations in the structure of the collagen or its relationship to the mineral elements, but he believed that the explanation was to be found in the cells themselves. He described experiments designed to measure the force necessary to crush a vertebral body at various levels. Even in cases of osteoporosis a load of a third of a ton might be necessary; but

it was hard to imitate the conditions found in vivo, and results had therefore been difficult to interpret.

### Radioactive Isotopes and Bone

Dame JANET VAUGHAN (Oxford) pointed out that radioactive elements from the "fall out" which entered the body were concentrated in the skeleton, where they were manifested by the production of anæmia, certain changes in the bones themselves, and the production of neoplasms. The vital factor was the radiation dosage; once the element was within the bone the important factors were the character and the energy of the radiation, together with the half-life of the element and the character of the decay products. All investigations had been complicated by the large number of variables. There were pronounced inter-species differences in resistance; and other important factors included the amount ingested, the route of ingestion, the diet at the time, the duration of ingestion, the site of deposition, and the pattern of subsequent bone growth. In describing experiments with $^{90}Sr$ in the rabbit, she showed how the age of the rabbit controlled the pattern of deposition in accordance with the site and rate of bone growth at the time; it was the local concentration of a radioactive element that led to the danger of tumour-formation. Work on these extremely complex problems was still at a very early stage, and it was rash to assume that the behaviour of one radioactive element would prove similar to that of any other.

### The Short Leg in Poliomyelitis

Mr. A. H. C. RATCLIFF (Manchester) had measured radiographically the shortening of the leg after an attack of poliomyelitis confined to that limb. Shortening was greatest in patients infected at the age of about 3 years, and was rare in patients infected after the age of 8. Only 6 of the 220 cases analysed had no resultant shortening. In only 1 was the shortening more than $3^1/_2$ in. In general, the more severe the paralysis the greater the shortening. In 94%, both femur and tibia were involved, in most instances the tibia being the more severely affected. In only 1 patient was the femur alone shortened. The disparity started to appear without delay after the illness. Patients could be divided into three groups according to their subsequent progress: (1) a severe group where the disparity increased steadily to about $2^1/_2$ in. during the subsequent nine years; (2) a milder group where deterioration was slower but still progressive; and (3) a group in which shortening progressed to $1–1^1/_2$ in. in a few years, after which the disparity remained constant. The discrepancy never became less. Children infected in the 0–2 and 4–7 years age-groups showed no significant differences in the subsequent shortening. Prognosis was difficult; where the paralysis was confined below the knee the greatest shortening seen was $1^3/_4$ in., there being no apparent difference whether one or more muscle-groups were affected. Where muscles were involved both above and below the knee, severe paralyses might involve shortening up to $3^1/_2$ in. But severe paralysis had been seen with only slight shortening.

Mr. J. I. P. JAMES emphasised that radiographic measurement was essential, though clinical examination must be added to exclude such contractures as could produce foreshortening of the bones and therefore misleading radiographic appearances. He agreed that, in general, the worse the paralysis the greater the shortening, but he had seen 1 case of a totally paralysed leg 1 in. *longer* than its normal fellow.

Mr. RATCLIFF remarked that Green of Boston had noted lengthening in a paralysed limb during the first two years after the disease, but this had always proved a temporary phase.

### Treatment of Perthes' Disease

Mr. D. L. EVANS (Southend) and Mr. G. C. LLOYD-ROBERTS (London) had compared the results of treating patients with Perthes' disease as outpatients, by means of a Snyders' sling and crutches, with those obtained by traction in bed, followed by walking in a weight-relieving calliper. From the outpatient group 28 boys with unilateral disease were selected; the radiographs of each were matched with those of a boy of similar age and stage treated as an inpatient. The results in the two groups were almost identical, and showed no significant difference whether age or stage of the disease was considered. The clinical features had been shown to parallel closely those of the radiographs. In view of the obvious social and economic advantages they therefore considered that outpatient treatment was the method of choice.

### Stress Fracture of the Tibia in Athletes

Mr. M. B. DEVAS (Hastings) said that "shin soreness" in athletes was a well-known condition of insidious onset starting towards the end of a run and eventually becoming severe enough to prevent further running. Rest relieved symptoms, but these recurred as soon as the patient tried to run again. He believed that these symptoms were caused by a stress fracture of the tibia—difficult to diagnose because it was partial, involved one cortex only, and was very late to show radiologically. Typical cases diagnosed and treated early might never attain the stage of radiological confirmation, which had been seen in 16 patients. The fracture was usually at the junction of the middle and lower third posteromedially, in contrast to that seen much more commonly, typically in recruits, which affected the upper third. According to Burrows, stress fractures in ballet dancers affected the middle third. Local tenderness and œdema were present early, and later definite thickening of the subcutaneous surface of the tibia. There was slight subperiosteal new-bone formation, and later a fine fracture-line running usually upwards and inwards from the posteromedial cortex. The fracture might remain invisible even three months after the onset of symptoms. Repeated bending of the tibia due to powerful calf muscles was the suggested mechanism. In treatment rest from running was essential; strapping support was helpful, and in some a few weeks in a below-knee walking plaster was necessary. Training must be restarted gradually.

Mr. NORMAN CAPENER (Exeter) was installed as the new president.

## New Inventions

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essentially of two small file-like surfaces on the slanting tip of a pair of curved forceps (see figure). As the forceps are closed, these rough surfaces catch the membranes and bring them together in a fold, which is held by teeth between the jaws. They work easily even when the membranes are closely applied to the fœtal head.

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# Reviews of Books

## Principles of Surgical Physiology

H. A. DAVIS, M.D., C.M., F.A.C.S., clinical professor of surgery and director of surgical reseach, College of Medical Evangelists, Los Angeles Division. London and Toronto: Cassell. 1957. Pp. 841. £7 7*s*.

IN a foreword, Dr. Lester Dragstedt observes that "The remarkable progress in the science and practice of surgery during the past twenty years is largely due to a better understanding of physiologic principles by surgeons"; and in this book Dr. Davis attempts "to organise those physiologic facts and concepts which the surgeon needs in his daily work." The first and smaller section is concerned with general principles, and there follows a more detailed system-by-system discussion.

The scope is much wider than the title suggests: not only the normal physiology of each system is described, but also pathological disturbances of function and the results of experimental surgery. In this endeavour to relate the abnormal to the normal, the book attempts a valuable and potentially fertile synthesis, but its impact is weakened by the inclusion of much irrelevant material of purely clinical, operative, or pathological significance. This is an unwelcome aside from the main purposes of the book, and it also results in a disappointingly superficial and dogmatic view of the fundamental physiological processes. The value of the book would be much enhanced by judicious pruning and expansion.

Dr. Davis is to be congratulated on his comprehensive and essentially up-to-date review of so vast a subject. Nevertheless, this single-handed approach has disadvantages, and even though the text has been criticised by a formidable panel of experts the specialist in a particular subject would no doubt differ from Dr. Davis on many points, particularly in the matter of emphasis. Containing a great many facts, with a good bibliography at the end of each section, this book should prove a useful reference volume to the research-worker; and, read with discretion, it can help all surgeons to understand more of the physiological basis of their craft.

## B.C.G. Vaccination Against Tuberculosis

S. R. ROSENTHAL, M.D., PH.D., Director, Institution for Tuberculosis Research, University of Illinois. Boston: Little Brown & Co. London: J. & A. Churchill. 1957. Pp. 389. 55*s*.

## Advances in Tuberculosis Research

Vol. 8. *B.C.G.—A Discussion of its Use and Application*. Editors: Dr. HANS BIRKHÄUSER and Dr. HUBERT BLOCH. Oxford: Blackwell Scientific Publications. 1957. Pp. 318. 60*s*.

Dr. Rosenthal's book seems to have appeared in response to the increasing attention being paid to B.C.G. vaccination in the United States. There is no doubt that, as is implied in the foreword, the United States has lagged far behind other countries in using this effective preventive measure. But the book is not for domestic use only. It is similar in plan to Irvine's excellent book published in this country, but it contains rather more detail. Some might wish for more criticism of the less scientifically valid investigations of the past; but the book is certainly not special pleading and the evidence is adequately and fairly presented. Chapters by three of the pioneers of B.C.G. vaccination—Guérin, Weil-Hallé, and Wallgren—add extra interest.

The latest volume in the *Advances* series is a collection of authoritative articles, in general well written and pleasingly produced. It includes an assessment of the first results of the Medical Research Council trial by D'Arcy Hart and his colleagues, articles by, among others, Bloch, van Deinse, Rosenthal, Birkhaug, the late A. Q. Wells, Aronson, and Dahlstrom, and a critical summary by Myers of the views opposing B.C.G. vaccination.

Dr. Rosenthal's book is primarily for clinicians and public-health specialists; the *Advances* volume is mainly for the few who wish to inquire more deeply into particular aspects of the subject.

## Aortography

W. BARR STIRLING, CH.M., F.R.C.S.E., F.R.F.P.S.G., senior assistant, urological department, Glasgow Royal Infirmary. London and Edinburgh: E. & S. Livingstone. 1957. Pp. 289. 50*s*.

THIS book is principally concerned with the application of aortography to urological diagnosis. The history and techniques of aortography and some of its potential hazards are ably described. Brief case-histories illustrating renal lesions, and the relevant nephrograms, are included, and where appropriate the relation of the vascular picture to urography is established. Less space is devoted to aortographic changes in some of the arterial diseases involving the aorta and the peripheral vessels. The text is lucid and stimulating; and the reproductions are superb. While many surgeons and radiologists may be a little reluctant to apply aortography as widely as Mr. Stirling does, few will deny that it is now an established part of urological diagnosis; and this monograph is a valuable guide to radiologists and surgeons.

## One Surgeon's Practice

FREDERICK CHRISTOPHER, M.D., emeritius professor of surgery, Northwestern University Medical School, Philadelphia. Philadelphia and London: W. B. Saunders. 1957. Pp. 151. 28*s*.

Dr. Christopher really needs no introduction in this country to those who have graduated during the past two decades (*Minor Surgery* and his larger textbook are widely known); nevertheless here he engagingly introduces himself.

The early chapters give facts and advice to the intending surgeon; and in doing so they provide a source of material for the sociologist delving into medicine (for one thing, the average hours worked per week in the various surgical specialties would make a trade-unionist blanch). Here also is sound advice often of an unusual kind; the young surgeon is advised to consider the necropsy-rate at a hospital before applying to join the staff—a figure below 50% indicating low professional standards. On what to tell the patient, the explanation of so simple a condition as hernia seems overdone; but it is a delight to find later that the American patient, like others the world over, when "... asked to lie down on the table, he will lie on his back, but if he is told to lie on his back, he will, for some unknown reason, lie on his stomach."

As the book progresses, Dr. Christopher lapses unashamedly into reminiscence; his anecdotes reveal the man—his sympathy, his dry humour, even very occasional anger. Dr. Christopher has a bear story which he recites to distract the attention of young patients he is examining; and it is so fascinating that it must always be finished. He has now written another bear story.

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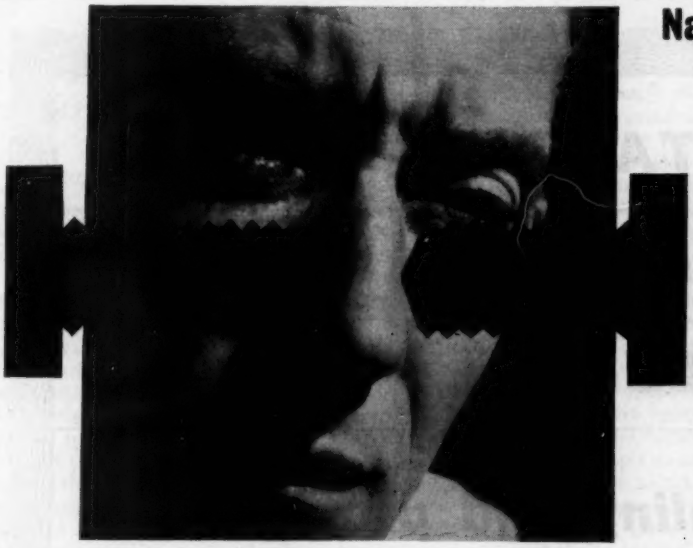
**Diseases of the Nose, Throat and Ear** (10th ed. London: Henry Kimpton. 1957. Pp. 968. £6 6*s*.)—This firmly established shorter textbook of otolaryngology, whose principal authors are Prof. H. C. Ballenger and Dr. J. J. Ballenger, of Northwestern University Medical School, Chicago, celebrates its half-century by a tenth edition. It is attractively printed and generously illustrated. Much space is properly devoted to the complications of middle-ear suppuration. The otologist may occasionally have to treat a cerebral abscess, but some of the techniques described here would not meet with neurosurgical approval. Surgery is given pride of place in the treatment of carcinoma of the larynx, and insufficient emphasis is laid on the close cooperation between laryngologist and radiotherapist that achieves the best results. The section on endoscopy is by Tucker, Chevalier Jackson, and Atkins—a team whose names alone are commendation enough.

**Skin Diseases for Beginners** (London: H. K. Lewis. 1957. Pp. 43. 7*s*. 6*d*.).—This little book by Dr. R. B. Coles and Dr. P. D. C. Kinmont offers some knowledge of the commoner skin diseases to nurses and others who need simple general information. The text is largely in the form of lecture notes, illustrated by line drawings of the anatomy of the skin and the distribution of lesions. The whole is easily assimilable, instructive, and unburdened with jargon. The authors have succeeded in their difficult task, but their book deserves a stronger cover since it is likely to be much used in the libraries of nursing schools.



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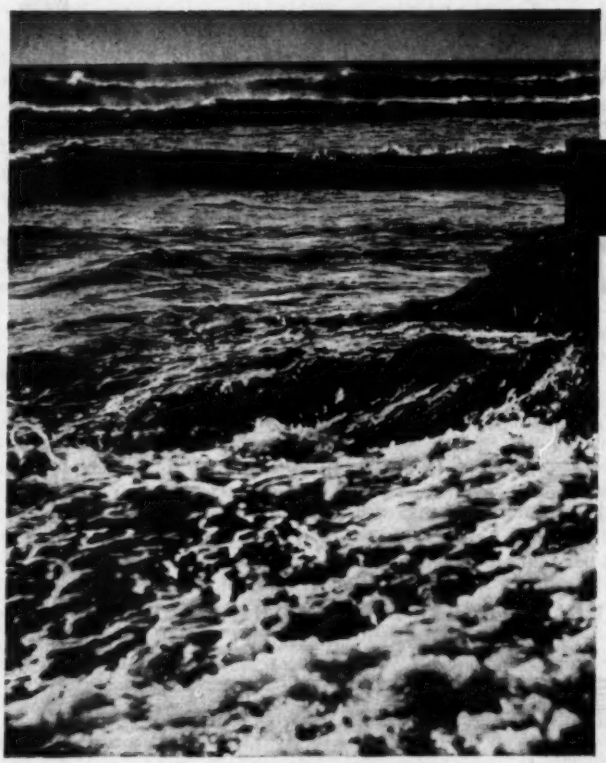

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# THE LANCET

*LONDON: SATURDAY, NOVEMBER 16, 1957*


## Treatment of Undescended Testis

UNDESCENDED testes may enter the scrotum spontaneously at any time from infancy to manhood. More than 10% of testes are undescended at birth, but only 2% remain outside the scrotum at puberty, and in mature men the proportion is as low as 0·2%.[1 2]

Such evidence as there is suggests that fertility is satisfactory in men whose testes have descended spontaneously before puberty. HAND [3] observed six patients with bilateral undescended testes in whom one or both testes descended between the age of 9 and 13 years; all have been fertile in marriage. WILKINS [4] states that testes that remain in the inguinal canal or abdomen throughout childhood and then descend spontaneously are "apparently always normal." If the truth of this assertion could be confirmed in a large series there would be less enthusiasm for any sort of intervention before puberty. After puberty the cryptorchid testes, whether in the abdomen or in an ectopic position, degenerate and atrophy; and if the cryptorchidism is bilateral the man is likely to be irreclaimably sterile. If one testis is in the scrotum by puberty and the other is not, then operation may be recommended, to prevent the risk of later malignant change in the undescended testis. BAKER [5] is the chief protagonist of the view that the incidence of cancer in the cryptorchid testis in later life (11% according to his figures) is so high that orchidectomy should be recommended for the cryptorchid testis. CARROLL [6] rejected this estimate after circularising all urological surgeons in the United States. He believes that the risk of cancer should not influence the treatment of undescended testis. A reasonable compromise between these two views is possible: if after puberty a testis is shown by biopsy to be irreversibly degenerate it should be removed; if there is a possibility of its functioning normally, orchidopexy should be done and the very slight risk of cancer in the scrotal testis should be ignored.

A more important debate concerns the age at which it is right to intervene in bilateral cryptorchidism. Here again there is not enough evidence to justify dogmatism. It is generally agreed that up to the age of five to six years the undescended testis does not differ in structure from its fellow in the scrotum. From this age until puberty the undescended testis shows some tubular immaturity, perhaps with peritubular fibrosis.[7–9] Both the immaturity and the fibrosis have been ascribed to the effect on the testis of a "hot climate," 1·5°–2°C above scrotal temperature, together perhaps with gonadotrophins, which, if there is also androgen deficiency, may be present in excess. This effect, long recognised in animals, usually proceeds to total degenerative change if the testes remain indefinitely in the inguinal canal or in the abdomen.[10] HELLER et al.[11] have shown that peritubular fibrosis is not irreversible in laboratory animals; so subsequent placement of the testis in the scrotum and an increased androgen output may produce a testis normal in both function and structure. SCOTT,[12] who is examining by biopsy a series of bilateral undescended testes, performing orchidopexy on one side at an early age and leaving the other testis until puberty, states that there is no difference between the histological appearance of the two testes at puberty. Likewise, ANDERSEN et al.[13] found no degenerative changes in biopsy specimens of cryptorchid and ectopic testes up to the age of fourteen years. SOHVAL [14] states that, while about half of 42 cases of undescended testes histologically examined showed only tubular immaturity, some testes examined near puberty showed germinal aplasia and others showed the rudimentary appearances found in a hypogonadal adult. He regards these changes as evidence of testicular dysgenesis—a primary disorder—and, if this were true, about half the testes still undescended at puberty would not benefit by either surgical or hormonal therapy.

Some workers [10 15] have concluded from these divergent histological observations that it would be well to perform orchidopexy before the age of five or six years, in order to prevent immaturity and peritubular fibrosis in the prepubertal period. This opinion is based on the expectation that the testis has a better chance of developing if in the scrotum; but it ignores the fact that the majority of undescended testes descend in any case before puberty, and also the possibility that some testes which are so brought down may already be affected by a genetic or environmental disorder that precludes fertility. Moreover, ROBINSON and ENGLE [8] recognise, ominously, that "some of these testes will be sacrificed because of the difficulty of surgery in this age group." The risk of damage to the testis by surgery has not been satisfactorily assessed. HANSEN [16] examined 25 bilaterally cryptorchid men who had been treated by orchidopexy and found that 14 were sterile and another 9 had some impairment of sperm formation; and CHARNY et al.[7] found definite deterioration of the seminiferous epithelium in the "majority of instances" after successful orchidopexy. These workers regard orchidopexy either as unjustifiable or as an operation to be done only as a "last resort" in bilateral cryptorchidism. Atrophy of the testes as a result of surgery involves both eunuchoidism and sterility, whereas sterility alone is the usual fate of men with undescended testes. Other reports give a better prognosis for surgical treatment. MACCOLLUM [17] followed up 22 patients treated by orchidopexy and found that, judging by sperm-counts, 15 were definitely fertile; of these 15, 6 were married and had children. HAND [3] reported that of 14 patients treated by bilateral orchidopexy before


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12. Scott, W. W. Cited by Wilkins (footnote 4).
13. Andersen, H., Andraessen, M., Quaade, F. *Acta. endocr., Copenhagen*, 1955, **18**, 567.
14. Sohval, A. R. *J. Urol.* 1954, **72**, 693.
15. Robinson, J. N., Engle, E. Pediatric Urology; vol. 2, p. 729. Philadelphia, 1955.
16. Hansen, T. S. *Acta chir. scand.* 1946, **94**, 117.
17. MacCollum, D. W. *Arch. Surg.* 1935, **31**, 290.

puberty, 5 were married, and, of these, 4 had children. Even if these more sanguine reports of the success of orchidopexy are accepted—and this would seem reasonable—possible damage to the testes by surgery may make the pædiatrician and the physician disinclined to suggest orchidopexy at an early age. Many workers favour orchidopexy at a later age; some would advise it at the age of eight to ten years,[1 3] others when puberty is established.[4]

As a prelude to surgery, most workers advise hormonal treatment.[1–3 14 18] In some cases this therapy alone leads to descent of the testes, and operation is thereby avoided. With such treatment the testes are exposed to a stimulus comparable to that which they would normally have received later at puberty, and it seems reasonable to conclude that the testes which descend would have descended at puberty. Hormonal treatment, like orchidopexy, is not universally approved. WILKINS[4] believes that such therapy may itself damage the testes,[19] and states that he has seen a "number of young men" who had been treated for cryptorchidism by chorionic gonadotrophin with apparent success but who were later found to have Klinefelter's syndrome of hyalinisation of the seminiferous tubules. It may be possible to avoid this danger by short, intensive courses of chorionic gonadotrophin. ROBINSON and ENGLE[15] administer 4000 units daily to a total dosage of 12,000 units. HAND[3] recommends 4000 units thrice weekly to a total dosage of 40,000 units. SPENCE and SCOWEN[18] recommend doses of 500 units—a recommendation supported by BISHOP,[1] who, in 139 cases, administered an average total dosage of 10,000 units. In cases where the testes can be palpated, hormonal therapy before puberty is likely to succeed.

Thus no absolute rules can be laid down for the treatment of bilateral undescended testes. Those who prefer to postpone operation until the age of eight to ten years, preceding this with a short intensive course of gonadotrophin therapy, can be reasonably certain, with expert surgery, of not doing their patients harm. But those who choose to postpone surgical treatment till puberty cannot be accused of neglecting their patients' interests. Whenever surgical treatment is undertaken, a biopsy examination of both testes should be made. If all cases, however treated, are carefully followed up, both by examination of the semen after puberty and by seeking evidence of fertility after marriage, we shall not only gain valuable guidance on treatment but also learn what proportion of undescended testes are the seat of irreversible genetic or environmental change, and how many are damaged by surgical or hormonal treatment.

## Accidents on the Road

IN many little ways, as Mme. DU DEFFAND observed, men differ from sheep; but the urge to exist and migrate in crowds is not one of them. Hence one of the most acute social, economic, engineering, and medical problems of our age—road traffic. We have lately referred[20] to attempts in the United States to study traffic accidents by epidemiological methods.[21 22] The Cornell University team have now published some of their findings, based on a painstaking analysis of many thousand accidents.[23] Over 2000 accidents were investigated with the specific object of determining those features of car design that are most commonly responsible for injury. The list is headed by the steering wheel and column, which were incriminated in 29% of all injuries. Ejection took second place; but it was second to none in the severe-to-fatal injury group. Other important items included the instrument panel, the windshield, the backrest of the front seat (especially its top portion), and the door frames. It is gratifying to learn that several manufacturers have already modified designs to reduce the injury potential of these structures. This has provided the Cornell University team with an opportunity to test their findings by controlled statistical methods. The relevant data of 2750 car accidents, sustained over the past fifteen years, were carefully analysed: in 200 the cars involved were of the latest (1956) model and incorporated safety-locks, seat-belts, and other modifications designed to reduce the risk of ejection. It was found that there was a 10–15% drop in the incidence of doors opening in both roll-over and other accidents; that the incidence of ejection was decreased by 6% (actually halving the number of people ejected); and that dangerous-to-fatal injuries were reduced by 3%. Added weight is given to these figures by earlier studies of MOORE et al.,[24] who found no difference when cars manufactured in 1944–49 and 1950–54 were similarly compared. To test further the effectiveness of safety-belts the data of rural accidents, in which 300 cars with and 4000 cars without belts had been involved, were subjected to rigorous examination. 81 cars in each group were suitable for comparative analysis. In the control group (no safety-belts) some degree of injury had been sustained by 75% of the occupants, against 30% in the experimental group (cars with belts). Severe-to-fatal injuries were suffered by 4% of occupants in the control group, by only 1% in the experimental group.

The findings at Cornell University leave no doubt that epidemiological and statistical methods can usefully be applied to the study of road casualties; that prophylaxis can help greatly to reduce their number; and that collaboration between engineers, manufacturers, and doctors can make prophylaxis especially effective. Whether such a concerted effort can offset the growing density, speed, and power of motorised traffic remains to be seen; it seems likely that for many years to come road accidents will continue to increase in frequency and severity.

If manufacturers, designers, and the car-buying public are now beginning to heed medical advice on how to prevent accidents, doctors must turn with renewed interest to their actual management. There are, broadly speaking, three ways in which progress can be made. The first is by teaching and propaganda. The fundamental principles of dealing with the severely injured cannot be too widely disseminated; in first-aid treatment of road accidents every passer-by becomes a member of the "greater

18. Spence, A. W., Scowen, E. F. *Lancet*, 1938, ii, 983.
19. See Maddock, W. W., Nelson, W. O. *J. clin. Endocrin.* 1952, **12**, 985.
20. *Lancet*, Sept. 28, 1957, p. 627.
21. McFarland, R. A., Moore, R. C. *New Engl. J. Med.* 1957, **256**, 792.
22. Braunstein, P. W. *J. Amer. med. Ass.* 1957, **163**, 249.
23. Braunstein, P. W., Moore, J. O., Wade, P. A. *Surg. Gynec. Obstet.* 1957, **105**, 257.
24. Moore, J. O., Tourin, B., Garrett, J. W. A. Study of Crash Injuries Patterns as Related to Two Periods of Vehicular Design. Department of Public Health and Preventive Medicine, Cornell University Medical College, 1955.

medical profession." The second task is one of organisation: as Mr. LOWDEN wrote last year,[25] an efficient accident service, organised on a country-wide basis, is essential if the public is to receive the full benefit of new theoretical knowledge and practical skill. If much, or at least some, progress has been made along these two fronts, all is singularly quiet on the third. Many victims of road accidents still die between the time of the accident and their arrival in hospital; some arrive moribund; a few, to the despair of the surgeon, arrive desperately in need of, but unfit for, operative treatment. This is no criticism of the ambulance service, which on the whole works admirably. The fact is that war experience sometimes befogs our vision. Under front-line conditions rapid staged evacuation of the wounded is the secret of success; so essential is it that the question of whether it is medically desirable hardly arises In peace-time there are cases—for example, of suspected intracranial hæmorrhage—where immediate transportation, however great the risks, offers the best chance of survival. Yet there is no doubt that lives could be saved if removal to hospital was sometimes delayed long enough to allow an intravenous infusion to be set up on the spot. This would require the supply to ambulances of infusion apparatus and fluids and the attendance at serious and remote accidents of a doctor capable of judging when to wait for resuscitation and when to move the injured at once—a skilled decision. But there is no real reason why such provisions should not be part of an adequately staffed accident service; and the case is particularly strong in areas where casualties may have to be taken many miles to hospital. Resuscitation can be given on wheels, in the front-garden of a suburban house or in the backyard of a farm, as effectively as in hospital. It would clearly be unsound, however, to divert a large number of hospital staff to such "roadside" resuscitation duties, for many of the accidents could be dealt with perfectly well under existing arrangements. But when first reports suggest serious injuries and when there is a long way to go, a resuscitation team might be dispatched with the ambulance. Often enough its services would not be vital; but it would from time to time undoubtedly save life, and it would do away with the unhappy picture of an ambulance car trundling over bumpy country lanes, with a shocked patient hopelessly enclosed in it.

25. Lowden, T. G. *Lancet*, 1956, i, 955, 1006, 1060.

# Annotations

## MUSCLE FUNCTION AND POTASSIUM

A RELATIONSHIP between the function of cardiac muscle and the potassium content of its perfusing fluid was demonstrated experimentally by Ringer[1]; and the clinical relevance of a similar relationship in skeletal muscle was shown by Aitken et al.[2,3] in a patient with familial periodic paralysis. Later work has brought out some of the complexities in the relation of muscle function to potassium metabolism: not only may low levels of plasma-potassium be accompanied by no muscle weakness, but also paralysis, as well as the more usual paræsthesiæ, may be associated with hyperkalæmia.[4,5] The potassium levels accompanying hyperkalæmic paralysis have usually been very high—upwards of 8 mEq. per litre—and it has been suggested,[5] largely because of the association with paræsthesiæ, that this type of paralysis may represent a neuropathy rather than a primary affection of muscle. It is therefore uncertain how far sporadic hyperkalæmic paralysis is analogous to the interesting condition of "adynamia episodica hereditaria" reported in two Swedish families.[6] In this syndrome, spontaneous paralysis is associated with a relatively small increase in the plasma-potassium; attacks may follow exertion, and in one such attack there was striking muscle weakness at a serum-potassium level of only 6·8 mEq. per litre. Attacks have also been precipitated by quite small amounts (4 g. or less) of potassium chloride; electromyography showed a change in pattern "suggesting loss of active muscle fibres." The urinary potassium usually increased; so there was evidence of loss of potassium from cells, though not necessarily from the muscle-cells involved. The attack could be controlled by giving calcium intravenously.

The common discrepancies between plasma-potassium level and muscle-power have naturally focused attention on the intracellular potassium and also on change in the distribution of other ions, particularly sodium.[7] Many of the factors influencing the intracellular potassium content have been defined by observations on animal muscle, often in vitro[8]; but it is difficult to combine such observations with assessment of muscle function. Although the human forearm, by comparison with the excised frog gastrocnemius, is less patient of quantitative study of potassium shifts, it is also less remote from the clinical situation; and the studies of Grob et al.,[9] comparing arteriovenous potassium differences and muscle-function, form an important contribution to this vexing problem. Most of their findings, not surprisingly, were predictable from the experience with isolated muscle. For example, muscle contraction and the intra-arterial injection of acetylcholine were associated with release of potassium from the forearm; while oral administration of potassium chloride and arterial administration of adrenaline were followed by uptake of potassium, and in the resting state there was a small uptake of potassium by the forearm. While oral glucose by itself was associated with uptake of potassium, when oral glucose was followed by arterial injection of insulin there was discharge of potassium from the forearm on that side. Grob et al. suggest that when insulin is added to glucose the further lowering of plasma-potassium, by increased uptake in the liver, increases the efflux of potassium from muscle-cells by increasing the concentration gradient between intracellular and extracellular fluid. The uptake of potassium into the forearm after oral glucose could also be prevented by giving cortisone orally, or hydrocortisone hemisuccinate intra-arterially. Muscle function was studied in the same experiments by recording action-potentials and isometric tension during percutaneous ulnar-nerve stimulation; and the effect of acetylcholine and neostigmine given intra-arterially was observed, with intermittent nerve stimulation. It was found that in those situations where the ratio of intracellular to extracellular potassium had probably decreased, there was increased muscle contractility and readier depolarisation by acetylcholine; these changes are ascribed to a fall in resting membrane-potential. Conversely, in situations where the ratio of intracellular to extracellular potassium

1. Ringer, S. *J. Physiol.* 1883, **4**, 29.
2. Aitken, R. S., Allott, E. N., Castleden, L. I. M., Walker, M. *Clin. Sci.* 1937, **3**, 47.
3. Allott, E. N., McArdle, B. *ibid*, 1938, **3**, 229.
4. Finch, C. A., Sawyer, C. G., Flynn, J. M. *Amer. J. Med.* 1946, **1**, 337.
5. Bull, G. M., Carter, A. B., Lowe, K. G. *Lancet*, 1953, ii, 60.
6. Gamstorp, I., Hauge, M., Helweg-Larsen, H. F., Mjones, H., Sagild, U. *Amer. J. Med.* 1957, **23**, 385.
7. See *Lancet*, 1957, i, 824.
8. Fenn, W. O. *Physiol. Rev.* 1940, **20**, 377.
9. Grob, D., Liljestrand, A., Johns, R. J. *Amer. J. Med.* 1957, **23**, 340.

had probably increased, there was decreased ease of depolarisation by acetylcholine; no weakness of muscle could be demonstrated, but the lowering of extracellular potassium in these experiments was not great, and the change in concentration ratio may have been further limited by loss of potassium from the muscle-cells. These results on "experimental man" seem to provide a reasonable basis for at least some of the clinically observed variations in muscle-power at a given level of plasma-potassium.

When the same techniques were applied to patients with periodic paralysis [10] it was found that uptake of potassium was greater than normal, and occurred even with insulin + glucose—which in normal subjects had been associated with loss of potassium from the forearm. These findings are in general agreement with those of Zierler and Andres,[11] which included assessment of blood-flow but not of muscle function. During recovery from attacks of weakness potassium was discharged from the forearm, and this discharge was accelerated by exercise to a greater degree than in the normal subject.

These painstaking studies still leave many problems, the most obvious lacunæ being a more direct evaluation of intracellular changes, and some information on associated shifts of sodium. The reasonable agreement of the present results with animal studies suggests that these latter can be extended with fair hope of relevance to clinical problems. When the problems of muscle-weakness have been tidied up, perhaps someone will turn to producing an explanation of nocturnal cramps.

## RADICAL SURGERY IN SPINAL TUBERCULOSIS

CHEMOTHERAPY has enabled surgeons to treat tuberculosis of the spine more actively [12]; but the place of arthrodesis has not yet been defined. The spine is the one part of the skeleton in which healing of a tuberculous infection commonly leads to bony, as distinct from fibrous, ankylosis; and occasionally in an ambulant patient the whole cycle of infection is followed by vertebral union. Whether bony ankylosis is encouraged by an early posterior graft is debatable. In America early operative fusion has been held to promote healing and to prevent progressive deformity; but this view has never been widely accepted in Britain, where fusion has usually been delayed until the disease was quiescent. Even then it has usually been reserved for patients with an unstable spine, with progressive deformity, or with recurrent disease. There is little doubt that, after a successful posterior fusion in a child, the growth of the arthrodesed area is depressed, and the intervertebral-disc space is narrowed or obliterated. But Hallock et al.[13] have shown that the overall growth of the spine is only slightly retarded.

Recent interest in the direct approach to the affected vertebræ, with evacuation of the abscess and removal of infected bone, has led to the development of more extensive operations on the spine. Wide excision of necrotic tissue undoubtedly hastens healing and prevents further spread of infection; but the cavities which remain to be filled after adequate evacuation of an extensive lesion are formidable, and packing with bone chips provides only a partial answer. Hodgson and Stock [14] have described a method of anterior fusion which may hasten convalescence in these patients. After an extensive excision of all infected bone and necrotic disc material a bony strut is passed across the defect, and sprung into position between the bodies of the healthy vertebræ above and below so that it remains under compression. The strut, which may be taken from ribs or from the bone bank, is reinforced by small match grafts. The wide exposure displays the lesion adequately, and enables the spinal cord to be inspected if necessary; the graft should maintain spinal stability and hasten bony fusion. It is too early to assess the final effects of this operation, but the early results are certainly very encouraging.

10. Grob, D., Jones, R. J., Liljestrand, A. *ibid.* p. 356.
11. Zierler, K. L., Andres, R. *J. clin. Invest.* 1957, **36**, 730.
12. See *Lancet*, 1957, i, 1230.
13. Hallock, H., Francis, K. C., Jones, J. B. *J. Bone Jt Surg.* 1957, **39A**, 481.
14. Hodgson, A. R., Stock, F. E. *Brit. J. Surg.* 1956, **44**, 266.

## "METABOLIC INSUFFICIENCY"

ABOUT a year ago we commented,[1] without enthusiasm, on the concept of "metabolic insufficiency" or "non-myxœdematous hypometabolism." [2 3] This syndrome is supposedly characterised by a low basal metabolic rate (B.M.R.), which responds to triiodothyronine but not to thyroid extract or thyroxine; direct tests of thyroid function give normal results. Its symptoms are said to include "lethargy, easy fatigability, nervousness, irritability, emotional instability, sensitivity to cold, headache, ill-defined skeletal pain, diminished sexual potency in the male, and menstrual irregularity in the female." The list includes many very common symptoms; and we therefore deplored a suggestion that doctors should try the effect of triiodothyronine (a potentially dangerous drug) on anyone who complained of them.

A further article has now appeared in which Morton [4] describes a study of 51 patients whom he regarded as having metabolic insufficiency. The protein-bound iodine in the serum was normal in all cases. The B.M.R. ranged from −40% to +2%; but "even though the B.M.R. was normal in some cases, if signs and symptoms of metabolic insufficiency were present, such cases were included." 36 of the patients had previously been treated with desiccated thyroid, thyroglobulin, or thyroxine; but only 3 had had a "good" response to this treatment. Triiodothyronine was started one to three weeks after the previous medication was discontinued. The results of treatment were assessed by the effect on symptoms, and were graded as "excellent" or "good" in 46 out of the 51 patients; the "most common and beneficial response was loss of fatigue."

Morton's study was concerned with the relative effect of two substances—desiccated thyroid and triiodothyronine—on a group of subjective symptoms. This is reasonable enough; for symptoms are after all what we aim to relieve, and the effect of medication on such things as the B.M.R. is, from the patient's point of view, of little consequence. But if symptoms are to be the end-point of a scientific trial, certain precautions must be observed in order to avoid error from bias on the part of either patient or observer. It is—or should be—universally recognised that when patients are given a new treatment many of their symptoms disappear, whatever the nature of the treatment. This can easily be demonstrated by the use of placebos. If Morton's patients had been given inert tablets, instead of triiodothyronine, it is to be expected that a large proportion of them would have felt better. An equally serious source of error in an investigation of this type is unconscious bias on the part of the investigator who is recording the patients' description of their symptoms. Much depends on how questions are put to the patient, and on what part of their answers is considered relevant. No-one, however conscientious, can safely feel that he is immune from bias in a matter of this sort. Such considerations have led to the technique of the "double blind" trial, which ensures that throughout the period of investigation neither subject nor investigator knows what medication is being given. In this particular instance tablets of identical size, shape, colour, and taste would have to be prepared beforehand—some inert, some containing thyroid extract, some containing triiodothyronine. They would be given to the patients in random order for

1. *Lancet*, 1956, ii, 826.
2. Kurland, G. S., Hamolsky, M. W., Freedberg, A. S. *J. clin. Endocrin.* 1955, **15**, 1354.
3. Tittle, C. R. *J. Amer. med. Ass.* 1956, **162**, 271.
4. Morton, J. H. *ibid.* 1957, **165**, 124.

predetermined periods; and the effect on symptoms would be recorded, and the trial completed, before the key was broken and the investigator knew what substances individual patients had actually received.

Obviously, this technique of the "controlled clinical trial" has not achieved wide popularity; and yet no other sort of trial concerning patients' symptoms is worth conducting at all. "Metabolic insufficiency" will remain an unconfirmed idea until investigated in a controlled study.

## POLYCYSTIC DISEASE OF THE KIDNEYS

WITH a view to finding out more about the genetic and clinical picture of polycystic disease of the kidneys, Dalgaard [1] has surveyed all cases in Copenhagen in 1920–53. He discusses separately polycystic kidneys in adults, on the one hand, and the congenital form in infants and children on the other.

Of the adult form his material comprises 242 reported cases and a further 108 cases found by personal examination of 3445 members of their families or their medical records. In Dalgaard's opinion, polycystic disease in the kidneys should always be regarded as bilateral, though of 32 patients submitted to nephrectomy only 8 died shortly after operation and others lived for many years (2 for seventeen years): of 183 necropsies and/or operations, in 14 cases one kidney was enlarged while the other was not. Other types of kidney cysts [2] were rigidly excluded from the material. Lambert [3] and Bricker and Patton [4] found that polycystic nephrons could contribute to the functional capacity of the kidneys; but Dalgaard is very critical about the significance of this finding, because the polycystic conversion leads to the patient's death, usually in uræmia. Of all Dalgaard's adult cases, 193 were in women, 157 in men; the mean age at the onset of symptoms was 40·7 years, at the time of diagnosis 47·2 years, and at death (254 cases) 51·5 years. The main causes of death were uræmia (59%), cerebral hæmorrhage (13%), and heart-disease (6%); other causes (22%) were varied and not significant. In 173 necropsies, cysts of the liver were found in 75 cases, subarachnoid hæmorrhage in 7, enlargement of the heart in 87, and renal calculi in 19; only 1 case of renal cancer and 1 of horseshoe kidney were found. The commonest clinical manifestations were pain and indefinite abdominal symptoms from an early stage, proteinuria, hæmaturia, and pyuria, palpable tumour, uræmia (usually insidious), and cardiovascular disturbances including hypertension. Pyelography was of great value in the diagnosis, and a combination of intravenous urography and tomography [5] seems to hold promise of even earlier diagnosis. Of the 193 women with polycystic kidneys 126 underwent 397 pregnancies, with 356 live births: only in 5 cases did renal complications develop during pregnancy. The prognosis was determined in cases diagnosed between 1920 and 1935. The duration of survival from the time of diagnosis varied from less than 1 year to 35 years. Dalgaard considers that treatment should be first and foremost medical, though surgical intervention may be necessary. Nephrectomy may be required for pyonephrosis; and persisting, incapacitating pain may call for multiple puncture of the cysts.[6] Otherwise, prevention of infection by avoiding catheterisation, correction of acidosis, avoidance of exertion, and other measures to prevent possible complications are the main measures recommended.

Dalgaard finds that in Copenhagen the risk of having polycystic disease by the age of 80 is hardly 1 per thousand, compared with 4 per thousand for thyrotoxicosis, 3·5 per thousand for epilepsy, 1·5 per thousand for mongolism, and 3 per thousand for hypospadias.[7] He concludes that in adults polycystic-kidney disease is due to a dominant gene which has an extraordinarily high penetrance. The relation to polycystic disease of the liver must be ætiological, and that to congenital aneurysms of the basal arteries of the brain is probably so. He suggests that a single gene causes these three malformations, with wide variation particularly in the liver and basal-artery components. He found no evidence of sex linkage, nor any sign of a close genetic relation with the blood-groups.

For the years 1911–53 Dalgaard found 40 cases in infants and 2 in children. These patients included 4 pairs of sibs, but no further cases were found among 310 family members. He accepts Potter's [8] division of congenital cystic kidneys into two forms—one in which the amount of renal connective tissue is normal, and one in which it is increased. From his material he concludes (though this cannot be taken as proved) that the former and commoner variety, producing enlarged "spongy" kidneys, is associated with a recessive gene, but the latter, with hypoplastic but irregular kidneys, is not genetically determined.

## PLEURAL NEOPLASM

MALIGNANT pleural neoplasm is one of the rarer causes of a straw-coloured pleural effusion, but this cause should be suspected if there is no evidence of a pulmonary lesion and the fluid becomes bloodstained or keeps accumulating after removal. If the fluid is replaced by air a chest film may demonstrate tumour masses on the parietal pleura (which is usually more heavily involved than the visceral pleura), although smaller lesions, visible at thoracoscopy, may escape detection by radiography. Material for histological examination may be obtained by blind needle biopsy or more certainly by biopsy under thoracoscopic guidance.

Embryologically the pleura arises from the mesoderm, and there has been considerable controversy as to whether these tumours are primary pleural neoplasms or secondary deposits. The variety of names that they have been given—mesothelioma, endothelioma, sarcocarcinoma—reflects differences of opinion about their origin. Smart and Hinson,[9] who describe 24 cases, conclude that, while it is impossible to deny that some of these tumours may originate in the pleura, there are few cases in which the evidence is incompatible with extension from a carcinoma. The primary carcinoma is usually situated in the lung, but it may arise in the stomach, colon, rectum, or breast. Bronchial adenocarcinoma, they believe, is especially likely to produce the clinical and pathological features of a "mesothelioma": it tends to have a longer natural history than other types of lung cancer; there is no great difference in sex distribution; it has a tendency to spread by the pulmonary lymphatics; and, most important, its cells seem able to use pre-existing structures as a stroma—for example, in the well-known case of so-called alveolar-cell carcinoma.

Owing to the widespread neoplastic involvement of the pleura the prognosis is hopeless, but Smart and Hinson report that by means of radioactive-gold therapy it is possible in a high proportion of cases at least to relieve the distress caused by persistent and copious outpouring of pleural fluid. In 10 cases they introduced 100 millicuries of radioactive gold into the pleural cavity, tilting the patient so as to distribute it evenly, and in every instance but one the rate of fluid formation was greatly reduced. Side-effects consisted in some general malaise, mild pyrexia, and slight pain and discomfort in the chest

1. Dalgaard, O. Z. *Acta med. scand.* 1957, **158**, suppl. 328.
2. Braasch, W. F., Hendrick J. A. *J. Urol.* 1944, **51**, 1.
3. Lambert, P. P. Le rein polykystique. Paris, 1943.
4. Bricker, N. S., Patton, J. F. *Amer. J. Med.* 1955, **18**, 207.
5. Evans, J. B., Dubilier, W., Monteith, J. C. *Amer. J. Roentgenol.* 1954, **71**, 213.
6. See annotation, *Lancet*, 1957, **1**, 679.
7. Kemp, T. *Cold Spr. Harb. Symp. quant. Biol.* 1951, **15**, 129; *Eugen. Quart.* 1954, **1**, 215; *Amer. J. hum. Genet*, 1954, **6**, 143.
8. Potter, E. L. Pathology of the Fetus and the Newborn; p. 368. Chicago, 1952.
9. Smart, J., Hinson, K. F. W. *Brit. J. Tuberc.* 1957, **51**, 319.

for two or three days. The gold remains radioactive for ten days; and due care must be taken in disposing of any fluid withdrawn during this period.

## CARDIAC ENLARGEMENT AFTER MYOCARDIAL INFARCTION

ENLARGEMENT of the heart following myocardial infarction is usually ascribed to factors other than the infarction itself—notably coexisting hypertension. But Master [1] has studied 600 cases of myocardial infarction and found that enlargement of the heart is fairly common in the absence of hypertension. Of the 500 men in his series, 45 had enlarged hearts with a normal blood-pressure. Of these 45, 16 had had heart-failure after myocardial infarction; but the other 29 had never been in heart-failure, although 2 had valvular lesions. "Hence the presence of heart failure or hypertension is not essential for the production of cardiac enlargement. It therefore appears that coronary sclerosis alone, without hypertension, can produce cardiac enlargement." Among the 100 women hypertension was much commoner than among the men; and cardiac enlargement after the infarction was also commoner both in hypertensive and in normotensive patients. Enlargement of the heart developed more commonly in elderly patients of each sex than in the younger. As myocardial infarction affects women on average 10 years later than men, it might be inferred that the age-factor alone would explain the greater liability of women to cardiac enlargement; but examination of Master's data shows that this is not the explanation.

Weiss and Weiss [2] followed the progress of 489 patients who survived acute myocardial infarction for at least two months and whose hearts were known to have been of normal size at the time of infarction. The period of observation varied from a few months up to 20 years, the majority of the patients being observed for several years. All the patients were examined fluoroscopically at least once, and most had several such examinations. In addition, teleradiographs were made of 129 patients to confirm the fluoroscopic findings. The heart was considered to be enlarged when the cardiothoracic ratio was greater than 0·5. Cardiac enlargement developed in 25 of the 489 patients, but in 15 there were factors which are usually taken as causes of an enlarged heart—namely, hypertension (13), calcification of the aortic valve (1), and unexplained cor pulmonale (1). In 8 of the remaining 10 patients no cause other than the previous myocardial infarction could be found. Congestive heart-failure was present in all these 8 cases, preceding the onset of cardiac enlargement in 4, all of whom had a myocardial aneurysm; while in the other 4 enlargement developed only after a second myocardial infarction. Weiss and Weiss conclude that cardiac enlargement due solely to myocardial infarction is rare. They emphasise the importance of myocardial aneurysm, which may develop at any time—even, in their opinion, some years after the myocardial infarction—and give rise to cardiac failure. The other few cases they regard as due to extensive myocardial fibrosis which weakened the left ventricle and induced congestive failure. "When congestive failure, which is a common complication of both these conditions, develops, the heart hypertrophies through as yet unexplained mechanisms."

Aneurysm of the heart is a much less uncommon complication of myocardial infarction than is generally realised. Thus Schlicter et al.[3] described 102 cases of ventricular aneurysm found at necropsy, representing a frequency of about 2% of all cases of myocardial infarction and 20% of those examined post mortem. The figure of 2% does not differ greatly from that of Weiss and Weiss for this complication. A large "through-and-through" infarct is especially likely to result in aneurysm. But Schlicter et al. found that a heavy load on the left ventricle in the first weeks after an infarction—for example, through early ambulation, coexisting hypertension, or valvular lesions—was an even more important factor. Because occasional patients with ventricular aneurysm have survived for many years, physicians have been inclined to regard an aneurysm as not worsening the prognosis. This view can no longer be sustained. Patients with aneurysm of the heart are more prone than others to have thrombo-embolic complications, but the really important cause of their poor outlook is the frequency with which congestive heart-failure develops in them. Recurrent infarction is also common; but, although the recurrent infarction often affects the same site, there was no rupture of a ventricular aneurysm in Schlicter's series. Excision of a myocardial aneurysm in 7 cases was reported by Likoff and Bailey.[4] 6 of the patients recovered, with relief of congestive failure, loss of gallop-rhythm, and arrest of paroxysmal arrhythmia. From their experience Likoff and Bailey suggest that the aneurysm should always be excised except when it involves the septum.

Cardiac enlargement after myocardial infarction, in the absence of hypertension and valvular lesions, is usually provoked by congestive failure. Dilatation may be supposed to be succeeded by compensatory hypertrophy. Initially such hypertrophy may enhance the power of the heart; but beyond a certain limit this does not hold true, because the capillaries of the heart do not multiply as the heart hypertrophies.[5] In any event it has apparently not been shown beyond doubt that hypertrophy of the heart-muscle is necessarily advantageous in permitting the heart to do more work.[6] An alternative hypothesis was put forward by Eyster,[7] who suggested that injury to the heart-muscle fibres, due to cardiac dilatation, was the essential prerequisite to hypertrophy; once hypertrophy was started, it continued in a self-perpetuating fashion even though the original provoking cause of the cardiac dilatation was removed. Such a mechanism would account for those few cases of heart enlargement after myocardial infarction where no other provoking cause is present. But Kerr [8] has re-examined this hypothesis experimentally and concluded that the evidence does not support it.

## A TELEVISION HAZARD

TELEVIEWING should, it seems, now be included in the list of hazardous occupations. Naide [9] described 3 patients of whom 2 developed a venous and the 3rd an arterial thrombosis in the leg while watching television for long periods. He suggests that the viewer, presumably fascinated by what he sees on the screen, remains fixed and immobile, thus encouraging venous stasis or arterial kinking. The belief that protracted recumbency in chairs or seats leads to thrombophlebitis is not new. Homans [10] emphasised the dangers of long automobile trips; Simpson [11] reported 21 sudden deaths from pulmonary embolism among persons in or leaving air-raid shelters; and Wright [12] pointed out the dangers of pressure in the folds of the groins from supporting garments such as girdles. Naide [9] believes that televiewers should train for their pleasure. Girdles and tight garments, he says, should be removed before viewing, the legs regularly moved during the performances, and a short walk taken every hour.

1. Master, A. M. *Amer. Heart J.* 1954, **47**, 321.
2. Weiss, M. M., Weiss, M. M. Jr. *Amer. J. med. Sci.* 1957, **234**, 129.
3. Schlicter, J., Hellerstein, H. K., Katz, L. N. *Medicine*, 1954, **33**, 43.
4. Likoff, W., Bailey, C. P. *Circulation*, 1956, **14**, 968.
5. Katz, L. N. *ibid.* 1954, **10**, 661.
6. Grant, R. P. *Amer. Heart J.* 1953, **46**, 154.
7. Eyster, J. A. E. *Trans. Ass. Amer. Physns*, 1927, **42**, 15.
8. Kerr, A. Jr. *Amer. Heart J.* 1957, **54**, 23.
9. Naide, M. *J. Amer. med. Ass.* 1952, **148**, 1202.
10. Homans, J. *New Engl. J. Med.* 1954, **250**, 148. See *Lancet*, 1954, i, 765.
11. Simpson, K. *Lancet*, 1940, ii, 744.
12. Wright, I. S. Vascular Diseases in Clinical Practice; p. 452. Chicago, 1952.

# The Wider World

## THE NEW CHINA

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(*Continued from page 939*)

### Into the Home

IN the old days the orders of the Emperor were conveyed to the uttermost parts of China by officials who received them at the great south gate of the Forbidden City in Peking. Today, this gate, Tien An Men, is the symbolic centre of the nation; and ceremonial parades are held before it, as in the Red Square of Moscow. Today, we are told, it is the centre of a nation in which the People, by democratic process, elect a Government to represent their opinions and aspirations—truly a People's Government.

Unquestionably the men thus elected to highest office—men whom even their opponents seem to respect—are very different from the Emperors, and from the former founders of new dynasties. On the other hand, we know that, in countries where information is controlled, the democratic process does not necessarily produce representative government: the process can indeed be made to go into reverse, so that the representatives represent the Administration to their constituents. Some observers hold that if Chinese government has changed in that it is now *for* the people, it cannot yet be said to be government *by* the pople. The rulers' edicts still issue from Tien An Men—though they have now become more pervasive and persuasive because voluntary workers help the officials to carry them into every home.

Reconstruction of a country of 600 million inhabitants requires not only a plan but also an instrument with which the plan can be fulfilled. The Communist Party is such an instrument, penetrating if sometimes a little blunt.

#### THE STREET COMMITTEE

It is a far cry from the fabulous throne-rooms of the Emperor to a slum in 6½-million Shanghai; but the slums are where people mostly live; and I want to introduce you to the chairman of a street committee.

He is a small worn man in early middle age—a pedicab driver.[15] Rescuing us politely from the tumult of children round the door, he gives us seats in the small whitewashed room which is the committee's headquarters. It has an electric-light bulb, some chinese lanterns, a blackboard, a telephone, and a few posters and notices; and someone has pasted newspaper over the rafters to brighten it up a bit.

His committee looks after a section of a district, and it is the representative body for about a thousand families—say 5000 people. Its three functions are (1) to administer welfare services, (2) to explain the policy of the Government, and (3) to reflect and transmit the opinion of the residents. The chairman, at any rate, seems to think of himself as chiefly representing his people, rather than authority. If the dustbins of his area are not cleared as usual at 5–6 A.M., the city office responsible will hear of it very soon.

I wanted to know whether the committee is genuinely elected, or in some way appointed from above: in Peking our informants had talked a little vaguely about elections without a show of hands. The system in Shanghai, he said, is that the people living in a courtyard or block—perhaps 17–20 families—elect a group-leader or warden. These group-leaders (about 50 of them) then gather in a large room, with a member of the district council in the chair, and elect the street committee: the one we visited has 13 members. The committee itself elects its chairman; and, since this is their "own people's organisation," the election needs no confirmation from above. The committee then forms five groups (each of 7 members, some coopted), to deal with welfare, culture, health, arbitration, and security. The cultural group tries to do something for the 20% of city children over 7 years old for whom no places in school can be found,[16] and for those who have left school but have not reached the age (18) when they can take a factory job; the arbitration group tackles disputes between neighbours; and the security group concerns itself with fire, thieves, and fighting.

As the medical authorities see it, the main function of the health group of a street committee is to "carry out the directives" of the city health office as regards sanitation, immunisation, and health propaganda generally. Having such close contact with people in their homes, they are in the front line of the patriotic health campaign; and in Shanghai the health office has in the past few years given no fewer than 50,000 such voluntary workers the elementary training they need as campaigners.

The slum we visited was pretty frightful, with earth tracks between the little houses—sometimes no more than hovels—and earth floors in the houses themselves. But it was under hygienic control. It was not squalid: there were no piles of refuse, no litter, no smells; and, though there were said to be some rats, there were hardly any flies. (This defeat of the flies, which astonishes every traveller in China, illustrates what can be done by a regime which can so easily enlist man, woman, and child against a common enemy. We could not help wishing that it would put the same zeal into a campaign against spitting, which is positively encouraged in some places by the profusion of spittoons.) Rubbish and night soil were regularly collected[17]; there were drains in the street, opening into sewers; and nearly every house had electric light. The 5000 people had to manage on 32 communal taps, but some of them got baths at their workplace, and they all seemed socially acceptable: the children, we were told, had baths in a basin every night.

Selecting a couple of houses at random, we found them clean and tidy—though one woman, with several children but only two rooms, complained of excessive housework. I asked her whether the street committee inspected her rooms to see whether they were up to the mark. "No," she said, "not the street committee: if the house were dirty, it's the neighbours who would criticise."—"But surely," I said "you'd be very angry if a neighbour came in and criticised your house!"—"No, no; it isn't like that here."

No: China is not in fact at all like middle-class England. For the poor in cities there is no privacy and never has been. (Even in a new model estate outside Shanghai, only families of six or more qualified for a *large* room; and the five housewives on the staircase shared a kitchen, though each had her own little stove.) Against this, there is *life*—in which everyone, willy nilly, participates. A birthday procession scatters the children in the narrow lane—the celebrants leaning back grandly in their pedicabs. Presently fire-crackers explode in all directions, disturbing the ducks. The children watch an old man making birdcages on his doorstep, or rush excitedly to see the visitors in a car. They block the road solid if one produces a camera. With life so abundant—and conversation incessant—perhaps even the aged seldom feel lonely.

As for the street committee, it is sometimes represented as the most terrifying organisation yet devised for Government interference with the lives of individuals. What hope has the rebel, or the fugitive, when none can

15. Pedicabs are the bicycle equivalent of a rickshaw. Nobody wants this undignified kind of man-drawn transport to survive, but existing pedicab drivers still ply their trade.

16. For the country as a whole the proportion is about 30%. Even so, there are now about 60 million children, aged 7 to 13, in primary schools in China—or rather more than the entire population of the British Isles.

17. Night soil is used as fertiliser. Dumped into piles, it becomes very hot, presumably sterile, and later friable, non-odorous, and convenient. Meanwhile the countryside often smells unpleasantly strong.

speak or stir within the street except under the watchful eye or ear of neighbours whose duty is to report him ? "[18] But in Shanghai we were told that the street committee does not report the presence of strangers—which must in any case become known in a few days when they apply to the police office for rations. I may be wrong; but, having seen something of what one street committee is up against and what it is managing to do, I am inclined to doubt whether the detection of traitors is one of its primary interests.

Indeed we left with considerable respect for this committee's work on behalf of the citizens, and also for its chairman; though the fact that he was wearing a badge lately given him by an Albanian football team suggested that he might perhaps be in the habit of explaining things rather well to foreigners. As for the myriad children—to whom we waved regally as they lined the route when the car drove off—they won our hearts by their welcome. But there again . . . perhaps they mistook Macaulay and me for Albanian footballers.

### THE WOMEN'S FEDERATION

Side by side with the street committee, the local members of a vast women's organisation, the All-China Women's Federation, work for the better health of women and children, and for the protection of women's rights. The law has given women equal status with men, and in large undertakings they have equal pay; but their equality is not yet fully understood by all employers, by all husbands and fathers, or indeed by all the women themselves. The Federation exists to fight discrimination everywhere; and its members, though they belong to different parties, nationalities, and religions, are at one in trying to mobilise women for the building of Socialism, to inculcate "both patriotism and internationalism," and to wipe out illiteracy.

### THE RED CROSS

A second unofficial organisation which we found giving very real help to people in their homes was the agreeably familiar Red Cross.

In Peking a local secretary and his wife received us in the bed-sittingroom in which they lived. Outside was the Red Cross station of the subdistrict—a small clean room with a stretcher, some diagrams on the walls, a cupboard full of first-aid remedies, and a pile of neat cheap handbooks on first-aid. In this subdistrict of 20,000 people, nearly 1200 have joined the Red Cross since Liberation, paying 15 cents a half-year for the privilege; and 240 have had a course in first-aid and hygiene, covering twenty-four hours, with an examination both written and practical.

One of the members thus qualified as "health workers"—usually a housewife, because she is likely to be at home—is in charge of each of the 15 substations, all in private houses and one in nearly every street. When there is an accident, people go to the nearest Red Cross substation, where, if the person in charge is out, they get help from some other member nearby. If need be, the stretcher is fetched, or the patient goes off to the doctor by pedicab.

The health workers are also on the lookout for communicable diseases, such as dysentery and encephalitis; and, though they do not undertake home nursing, part of their task is to explain how their neighbours can avoid harm—for instance, from heat in summer or from the carbon-monoxide poisoning too often caused by household stoves in winter.

Some of this street organisation recalls that of Britain in the blitz. The particular function of the Red Cross, working with the street committee, is to serve as "a link between layman and doctor."

## Primary Medical Care

In curative medicine three levels are recognised. From the doctors (traditional or otherwise) who correspond to our general practitioners the patient gets primary care. Or sometimes he may go direct to an institution on the second level—a hospital or clinic run by a city district or by a county. Or he may be treated at the highest level in one of the hospitals run by a city, a province, or a medical college.

By the look of things, primary medical care is eventually going to be given by Government-paid doctors in public buildings not unlike the health centres we hoped to have in Britain. But at present—even under official auspices—a modified private practice continues. It is another example of compromise.

A dozen doctors have formed a private group practice and occupy a fine European house in Shanghai. The fees they charge—higher than in Government clinics—require municipal approval; but otherwise they can make their own arrangements. They like being able to earn more by harder work, but they lack some privileges enjoyed by official doctors. They practise specialties; but the patient, if he wishes, can usually choose whom he sees. They are very busy but work only from 8.30 to noon and 2.0 to 5.30 and do no visiting or night work.[19] (Some of them, however, have their own personal practices as well.) Contact with a municipal hospital is close.

More altruism, and also far more official control, was evident in a group practice in Peking.

Starting in four rented rooms, the doctors at first spent much of their income on development; and thanks to Government loans, now repaid, they now have twenty rooms, with a branch surgery in prospect. The 12 of them (several traditional) serve a subdistrict of 40,000 people; they visit patients if necessary, and someone is on duty at night. New members of the group are chosen by the district health office, which also has the last word about the election of their two directors and decides their salaries—this year 150–200 dollars a month, with a small bonus for good work. Though as yet they do little preventive work except immunisation (for which vaccines are provided and the centre is paid 100 dollars a month) they hope to do more. The hours are 8.0 to noon and 2.0 to 6.0. The head nurse allocates the patients.

At Shenyang (Mukden) in the industrial North-East, private group practice has been abolished, and they are building municipal health centres.

The one we saw looks after some 25,000 (mostly privileged) people, including 5000 factory workers and others entitled to free medical care, and also their families, who pay half-fees. It is well staffed, with 16 doctors (1 traditional), nurses, laboratory technicians, 4 midwives, and 4 pharmacists, and it has an X-ray department. Doctors visit patients' homes, by bicycle, and one is on call at night.

This particular centre was called an "outpatient department" though it does not form part of a hospital. In cities primary care of exactly the same kind is often given in the outpatient departments of district (second level) hospitals, and we saw a good department of this kind attached to a new hospital in the rural outskirts of Shanghai.

But what seemed to me the best circumstances for primary medical care were found at the health centre of a Shanghai estate where 4000 families have lately been rehoused.

There are 5 doctors, 9 nurses, 4 midwives, 2 pharmacists, a technician, and 5 clerical workers. About 250 patients come each day, and the doctors are also medically responsible for two primary schools and a kindergarten.

The estate consists of three villages, to which the doctors and nurses are individually attached. At the centre a patient cannot be sure of seeing any particular doctor, but if he is seriously ill his own village doctor will visit him. Nearly all the babies born on the estate (two or three daily) are delivered in the six beds at the centre; antenatal work includes classes, in the Russian manner, preparing the women for "painless labour" without analgesics; and both mother and baby are followed up, well babies being brought to the centre at 6 weeks, 6 months, and a year. Records are good and improving; the doctors go to lectures at Shanghai hospitals;

18. A group-leader interviewed by de Segonzac said: "If I have the impression that there is a traitor in the street, then it is my duty, and that of all my fellow-countrymen, to denounce him immediately." (A. de Segonzac. *Visa for Peking*. London, 1956.)

19. Shanghai has an emergency station through which, if necessary, hospital doctors and ambulances can be summoned.

and they keep in touch with the hospitals by telephone, receiving reports on patients as soon as these are discharged. In the lobby were some instructive models for mothers to look at, showing (1) characteristic rashes and (2) examples of nourishing food.

I asked the director whether he meant to leave this work and pass on to something else. He said it was a new kind of job with a very wide range, which he found very interesting; and he hoped to go on with it. I was not surprised.

Primary medical care is also given at factories to the workers and sometimes to their families.

At a factory in Manchuria, where the 5800 workers produce an elaborate lathe every fifty minutes, there is a clinic (rather shabby) for the employees and another for their families, and also three "health points" in the works. The 11 doctors take duty in the shops, observing conditions and doing first-aid, and they also visit the homes.

At the huge automobile factory outside Changchun, where 55 doctors, 40 feldshers, and 170 nurses look after the 18,500 workers and their families, there is a clinic and maternity and child-welfare centre as well as a hospital of 300 beds. Each of the ten health points is manned by a feldsher and 2 nurses, and the clinic is for patients the feldshers cannot handle. The feldshers keep an eye on the workshops, and the doctors keep an eye on the feldshers.

At a cement works near Canton 1600 workers and their families are cared for by 5 doctors, and big new premises have been built for their clinic.

The smaller factories are often looked after by a local hospital whose doctors pay visits or staff a clinic. One of the district hospitals in Shanghai is responsible for medical care at no fewer than forty factories.

In the countryside the people depend mostly on traditional doctors, or else on nurses or feldshers, who may have to cover large areas. Western-trained doctors normally work in groups, not singly; but at the cooperative farm we visited in Manchuria medical work was shared between only two doctors—one modern and one traditional.

### In Hospital

Hospitals are multiplying fast: every county in China is said to have one now. But there are, of course, far too few. The 3 million people of Peking have only about 11,000 beds, and the 6½ million of Shanghai about 17,000.

In Shanghai most of these are in second-level hospitals controlled by a district health office; and an old one which we saw in the city itself, though enlarged since Liberation from 120 to 250 beds, was hard-pressed, with maternity cases at one end of a corridor and E.N.T. cases at the other. (They still have to deal with about 10 mastoids a month.) On the other hand, a new district hospital in the suburbs, with 110 beds, had good conditions for work, and its surgeons referred only neurosurgical cases to a higher level. They were using hypothermia.

Mostly it is the top-level hospitals run by a city or a province[20] or a medical college that do the specialised work. Thus a large hospital in Peking, built in 1879 and rebuilt in 1954, is a centre for eyes and neurosurgery throughout the region and also takes patients from other provinces. Peking has a fine new children's hospital of 600 beds,[21] and another for thoracic surgery which I understand is excellent.

None of us saw a mental hospital. The number of mental beds in Peking was variously mentioned as 500 and 1000; and in Shanghai the head of a medical college spoke of the "very great" need for a mental hospital of 600 beds which is to form part of his new medical centre. Earlier this year, Williams,[22] of Melbourne, found mental hospitals "mostly crowded, but no more so than many of ours, and treatment . . . largely along orthodox Western lines." But Chinese psychiatrists, capable though they were, seemed to lack any interest in child psychiatry. Is it possible, Williams asks himself, that the conditions of life enable the defective and dull to fit with less difficulty into the community, without the provision of all our special schools and grades?

"I wonder," he goes on, "whether we are justified in placing such stress on the significance of behaviour problems of childhood. Are they really trivialities, to be outgrown, with time and the common-sense approach of busy parents, and the intimate contact with all the facts of life inseparable from the crowded conditions of living in China? To this it seems should be added the supervision of the street committee, with the pressure it exerts on the wayward child and its parents, and the still dominant but disputed place of the grandparents in the family structure."

All I can add is the opinion (quoted to us) of a Chinese psychiatrist about British mental hospitals. When he visited one, he said, he could not see why some of the patients were there. They were just old people, sitting about, who would be better at home.

Though it is obvious that China can as yet offer only a small minority the kind of investigations and treatment customary in our own long-established hospitals, the developing medical centres at Shanghai and Canton, with big new special hospitals going up round the teaching colleges, induce the wistful incredulity which we English doctors nowadays feel at the sight of anyone putting up, for medical purposes, anything bigger than a glorified shed.

*Nursing*

Some difficulties, however, are international, and we were told in Peking that a number of beds are out of use because staff is so scarce. Women are encouraged to go on nursing even after marriage, and in a Shanghai hospital we heard how their tasks are lightened (no night duty and shorter hours) towards the end of pregnancy. In that hospital three-fifths of the nurses are qualified and two-fifths are assistant nurses who have been given only six months' training—some of them young girls and others elderly women.

To become a proper nurse in China, one must have a secondary-school education followed by three years' training, of which (if I can believe my ears) only six months is spent in hospital. On qualification they are, as a surgeon put it, "not very good." The unrealistic length of the theoretical training of nurses has been explained to me as due to a feeling that, in a world where everything is getting better, the work of the nurse should correspondingly become less material: after all, educated people in the old China took pains to avoid menially manual occupations. The upgrading of everybody seems to be a cosmic phenomenon.

*Anæsthetics and Drugs*

In one hospital we saw a nurse giving an anæsthetic, but usually this is done by a doctor. The Chinese have not copied the Russians' wide use of local anæsthesia, and they give a lot of open ether. Nitrous oxide and some other agents are scarce, and developments of inhalation anæsthesia to a British level will depend partly on improved supplies. But the Chinese would be greatly helped if some of our own anæsthetists would go and demonstrate exactly what we do.

Many other drugs (e.g., penicillin and P.A.S., and I think chloramphenicol) they are now making in quantity; but streptomycin, aureomycin, cortisone, and corticotrophin they still have to import—from Japan, Denmark, Poland and Britain.

*Administration*

A striking difference from English hospitals is in administration. As I have said, the control of the principal hospitals rests with the city, province, or medical college; but in the hospital itself administration is medical. The big general hospital we saw in Peking has a superintendent (a medical biochemist) who comes twice a week,

20. Administratively, the three biggest cities—Peking, Shanghai, and Tientsin—rank with provinces, and their districts with counties. Other cities rank with counties.

21. Former Western doctrine unfortunately prevails over the wisdom of the East, and there are only three visiting days for parents.

22. Williams, J. *Med. J. Aust.* Oct. 26, 1957, p. 630.

and six vice-superintendents (physicians, surgeons, and other members of the staff) each of whom looks after some large branch such as outpatients or children or surgery. To one of these vice-superintendents the matron is responsible. Similarly at the children's hospital the medical director deputes to colleagues certain large sections of his work—himself combining the special care of research with charge of some beds. In district hospitals, likewise, administration seems to be primarily by doctors.

### Clinic, Health Office, and Laboratory

Instead of going to a hospital, the patient may attend some kind of special clinic. In a big city this will usually be run by the people's council of his district—an area with perhaps 250,000 to 400,000 inhabitants. The people's council, which is the executive of an elected "people's congress" for the district, works through a district health office directed by doctors. This health office is responsible not only for medical care, at the primary and secondary levels, but also for what in Britain we call public health. Besides controlling perhaps a couple of general hospitals with anything up to 250 beds, it organises the maternity and child-welfare service, probably runs a clinic for tuberculosis, and has a district epidemiological station. This last—a useful importation from the Soviet system—is a district focus for preventive medicine.

One that we saw in Peking is quite big: it has a staff of 46, including 4 doctors, 16 nurses, 4 laboratory technicians, 6 sanitary inspectors, and 4 disinfectors. Its primary purpose is to control acute communicable disease, and in teaching people how to prevent infection it works with a district health committee (appointed after consultation) which has sub-committees in Government offices and factories. As part of the patriotic health campaign, war was declared on rats, flies, mosquitoes, and lice; and, by disinfection and disinfestation and baths, the public, like the streets, have been cleaned up.

The epidemiological station promotes immunisation, and supervises the hygiene of shops, restaurants, schools, and factories. Everywhere the idea is to enlist the help of the people themselves; and, if something is wrong in the hygiene of a canteen, news may well reach the station from workers in that canteen who have been taught to take an interest. But though the public are helpful, "they sometimes relax," and visiting of premises is necessary too.

The district epidemiological station will have a small laboratory; but the central epidemiological station for the city will have big ones. It will also conduct, at a higher level, the campaign of immunisation and environmental hygiene, including food and water supplies.

Thanks largely to the reduction of flies, and improved habits, food is safer. Inspectors take samples, and, if a shop or restaurant is recalcitrant, public opinion can be mobilised against it through the newspapers. Inside the walls of Peking 97% of the population now drink chlorinated city tap-water from artesian wells; and the water consumption, for all purposes, has risen from 19 litres per head daily before Liberation to 58.

In Peking (where T.A.B. vaccination is offered to some of the workers in food shops) typhoid now causes only a few cases each year. Though bacillary dysentery (87% of it Flexner) is more often reported than formerly, its fatality-rate is decreasing: amœbic dysentery is rarely seen. China has apparently been free from cholera since 1949 and from smallpox since 1950. In Peking relapsing fever has disappeared, and typhus has almost done so. In Shanghai notifications of cerebrospinal fever fell from 13·6 per 100,000 in 1953 to 6·6 in 1956.

This epidemiological transformation of huge Eastern cities would have been impossible, in so short a time, without the kind of personal instruction of the public—reaching their hearths and often their hearts—which is the main strength of the new regime. But it has also required intelligent organisation of medical resources which were often exiguous, and no small scientific competence in the workers who have had to produce some of these resources—notably in the six serum and vaccine institutes. These are not only centres of production but also centres of epidemiology and research.

The institute at Changchun, which has a staff of 550 and a library of 20,000 books and journals, started as a hygiene laboratory built by the Japanese in 1936 during their occupation of Manchuria. Under the technical control of a central body in Peking, it issues vaccines against smallpox, rabies, Japanese-B encephalitis, and plague; and it makes toxoids (diphtheria and tetanus), antitoxins (diphtheria, gas-gangrene, and botulism), and gamma-globulin from human placentas. It will shortly be producing B.C.G. A beginning has been made with tissue culture, and the virus studies in progress include experiments on a live influenza vaccine.

Because of the inevitable scarcity of trained scientists in China, this great institute had at first only four senior workers; and the younger ones have at present little chance of getting experience abroad—as the technical director, Dr. Chu Chi-Ming, did when for several years he was a valued member of the influenza team at our National Institute for Medical Research.

### Not yet Prevented

But, despite these victories on many fronts, some of the major preventable diseases are still very far from being prevented. Venereal infection, we were told in Shanghai, is "no longer a problem" now that prostitution has been suppressed; the infectious diseases of childhood seem to be under control in the cities; but large sections of the population are still exposed to serious risks, old and new, of which I shall give three examples.

#### SCHISTOSOMIASIS

Something like 11 million people—mostly in an area south of the Yangtse—are infected with *Schistosoma japonicum*.

The ova of this blood-fluke are passed in the stools and all too easily reach the innumerable cuts and ditches which intersect all that country for the soaking of the rice-fields. Once in the water, they enter a small snail, whence they return, in due course, as minute free-swimming cercariæ which will speedily penetrate the skin of anyone who wades at the water's edge or even wets his hand while filling a pail.

The resulting disease, often long postponed but eventually disastrous, can be treated, rather uncomfortably, with antimony. Given early, treatment can be preventive; and besides a large hospital for treatment of late cases we also saw a place in the country where a collection of cheerful children—most of them not yet ill—were living in an old family temple while they had their course of injections. A more radical form of prevention is to show the people how to avoid contaminating the water; but unfortunately such instruction does not influence their buffaloes, some of which are also infected. Or one can try to kill the snails, especially on the grassy banks of the canals and ditches where they commonly congregate.

In the Village of Seven Precious Things we watched a demonstration in which men with blowlamps burned off the grass, to the joy of the village children, some of whom nearly complicated the exercise by falling off the narrow stone bridges. This burning, with a mixture of carbon monoxide and petrol, can be done from a boat. Or, again, a spray of calcium arsenite can be used. Or, on a more primitive level, the children can be encouraged to pick up snails with chopsticks and put them safely in a jar.

The campaign to eradicate schistosomiasis within the next twelve years looks like being a campaign of attrition, in which no weapon is too small to be worth using. Something like 70,000 people have already been recruited for it.

#### TUBERCULOSIS

Deaths attributed to tuberculosis seem to have fallen recently in the principal cities. The mortality-rate in 1956 was given as 0·69 per 1000 in Peking (compared with 2·30 in 1949), and 0·63 per 1000 in Shanghai (compared with 1·64 in 1951). But a tuberculosis clinic in Peking, serving a district of 250,000, has 2700 patients on its register, and an intensive survey now being made in one of its subdistricts has revealed 30 cases among the first 1000 people examined. This being so, might it not be wise to ensure the widest possible distribution of P.A.S. and isoniazid by handing them out free of charge? Under comparable conditions in Thailand these drugs were

thought to reduce home infection because they so often reduce cough.[23]

As about 90% of Peking children are given B.C.G. at birth, and some get it later, I am not sure what to make of the fact that 30% of the 7-year-olds in this district are Mantoux-positive. It is noteworthy, however, that children in Peking have fluoroscopic examination on entering and leaving their primary schools, and more frequently in the secondary school. In a Peking general hospital the whole staff undergoes X-ray screening every six months—a practice which has now begun to look alarming.

At a factory in the North-East it was said that employees with open tuberculosis would always be sent to a sanatorium, run by the trade union, and would not be allowed to work. Sanatoria, however, do not yet seem to be a prominent feature of the medical service; and an unhappy state of affairs was evident at a cement factory near Canton where no fewer than 154 (over 9%) of the 1600 workers are tuberculous and there are only 40 beds for them. In this factory the tuberculous may be given lighter work, shorter hours, and a special diet, or may go to the sanatorium at night. But the workers' families had not been radiographed.

### DUST AND SMOKE

What we saw in that cement factory, and elsewhere, suggests that, in a country which is being industrialised so quickly, the new dust hazards require far more urgent attention than they are getting in China. Medical warnings, I should guess, are sometimes studiously ignored.

In the new department of industrial medicine at the Academy of Medical Sciences, pneumoconiosis is to be studied more comprehensively; but, though the building is large, the staff seemed small. A professor of public-health engineering in a Shanghai medical college, who was working on silica particles in crushed quartz, explained that since Liberation the medical authorities have been able to get into the factories, which previously took little pains to protect their workers: I think he said that, in one factory where quartz-crushing is done, no less than 38% of the workers had been found to have tuberculosis.

But adequate action does not necessarily follow recognition of a risk. An epidemiological station in Peking has found 37 dusty factories (stone, bricks, glass, lime) in its district of 350,000 inhabitants; and here the practice is for a doctor to go to the factory and ask it to make a plan for progressively getting rid of the dust. Often, I fear, the reply will be that nothing effective can be done till the factory is rebuilt. By way of secondary prevention, this station arranges for radiography for some 400 workers in dusty trades—once a year, or more often for people found to have lesions. At a lathe factory in the North-East the management were "very much aware" of the possibility of silicosis, though they said that at periodic examinations "not a lot" was found.

In all the three factories I saw there seemed to be some preventable dust hazards—much the worst being those in the cement factory in Canton, where the stone in use contains 20% silica and some of the men moving bags were quite insufficiently protected by their masks. On the credit side, this factory was about to spend about 2 million dollars, over two years, on fitting its chimneys with precipitators and fans to prevent the emission of dust, which has brought bitter complaints from farmers, hospitals, and schools for miles around.

Though they have not yet done much about it, the Chinese authorities are well aware of the harm done by atmospheric pollution, and in their new industrial cities plans for every factory must include "facilities for reducing chemical fumes and smoke." They also recognise the disadvantages of polluting rivers. But in all these matters—and especially pneumoconiosis—it seems urgent that they should make fuller use of what we have learnt so painfully in the West. At present they are buying their own experience needlessly dear.

*(To be concluded)*

23. Benatt, A. J. *Lancet*, 1956, i, 737.

# The Widdicombe File

## XLI. COMING UP THE EASY WAY

DEAR TOMMY,

Congratulations and commiseration, I hardly know which it should be—perhaps both. Congratulations on keeping your sights high, and maintaining your idealism; commiseration for the tough and at times frustrating life you will lead.

You may wonder why I mention idealism. It is because I appreciate that your decision to remain on the university side in clinical surgery stems from a number of highly laudable motives—a natural interest in developing your own subject, a hope of widening your own vision through university contacts, and a proper desire to influence the young in the right direction. And this you have chosen rather than the appointment to the part-time staff with its better financial rewards.

Of course, my assessment of your motive may be wrong. Perhaps you felt that your chances for the part-time staff in your teaching hospital had already been prejudiced by the grade-2 lectureship you have just held within the department of surgery. I do know of schools where this can be so; these are places (fortunately few) where the surgical staff speak of wanting a "practical man," thus insinuating that the research-worker is inept in the craft of surgery; where they prefer men "who have come up the hard way," the phrase being *applied* to those who have held their registrar appointments outside the professorial unit, and being *used* to infer that life on the unit is easy. In such a centre I have actually heard a candidate being recommended for staff appointment on the grounds of his toughness, the fact that he was a good fellow, and finally that he would *not* be likely to undertake any research. Irresponsible action for members of a teaching hospital, you may think; even more so when you consider that not one of what might be supposed to be the prerequisites for membership of what should be a learned professional body was even mentioned—nothing about intellectual capacity: no reference to contributions. To the candidate from the unit the attitude was rather different. "Mr. X, tell us, we would just like to know—what work do you do on the unit?" I don't need to tell you where the inflexion was placed in that question, nor of the insinuation.

If these are the circumstances you have found yourself in, then you have done right to elect to come on to the hospital staff from the university side as a senior lecturer. But I prefer to think that you chose this job for positive reasons and not simply to avoid identity with the backwoodsmen and the farmer-surgeons. When all is said and done, their behaviour is only protective—the cover-up of the craft-guild in the face of any challenge. And these men cannot appreciate that teaching hospitals are becoming university hospitals and that they, as a corporate body, are therefore being uplifted to university level. (This does not apply to London, where the university will never be any more than a name and a senate-house, and the hospitals will remain as teaching hospitals. However, London has other advantages.)

The conception of a university hospital is big—so big that I doubt whether it was in the minds of the Goodenough Committee, whose main purpose was to improve teaching and stimulate research, but who have nevertheless given us this priceless opportunity. To many who make use of the term it implies no more than the hospital which is attached to the university; but it is university hospitals in the grandest sense that we need to get us out of the deep furrows worn for us by the hortative and didactic forms of almost a century of medical instruction, to make us adaptable to our changing conditions, to provide scholars within medicine.

Yes, scholars, of a new sort. We are conditioned to thinking of the scholar as a man versed in the humanities; a man from whose lips classical tags trip lightly as insignia of his erudition; someone who can turn to the past in order to illustrate the present. But our scholar, our new man of university medicine, must be someone more positive who, while aware of the utter necessity of contributing to his subject, also maintains a breadth of horizon; whose sense of interest is fundamental and therefore attaches itself to any subject; who is able to infect others with interest and guide their minds over the barriers of demarcation so that, for example, surgery elides into medicine; who, added to all, has a strong liberal sense. Important that dash of liberalism; for professionally and by training we err towards being autocratic, a very unhealthy and limiting trait in a university mind. And, of course, our university man must have ideas.

What a paragon! What a hope! But what an ambition! Now you, my boy, could do all this, I am sure; but will you? You are now a senior lecturer and a consultant—one of those Goodenough boys. This means that your duties include the everyday routine associated with the care of the surgical patient, as well as teaching and research. This sounds reasonable enough, and not until you have tried it will you find it to be well-nigh impossible. The greater part of the week's timetable will be taken up with purely surgical affairs: this is inevitable and proper, for you will wish to hold your own with the "practical men"—more, you will take a pride in delivering a better, more efficient, and more human service than they. Routine lectures and teaching rounds take a further part of the normal working hours. The little that is left of the normal hours—and precious little it will appear—you will hopefully set aside for research. But you have forgotten that correspondence must be done in normal working hours when secretaries are available; that those references can be obtained only in normal working hours when the library is open; and that doctors will call you, instead of your house-surgeon, about some patient on the waiting-list, for it has got around that you are at the hospital all day and you are therefore thought to be a "whole-timer." You must spend time being helpful and civil because you are giving the best possible service. So, when 5 P.M. comes, your day really starts—on what you regard as the special work in your particular job; and you'll leave the hospital at 7.30 or 8 feeling a little worn.

You will have noticed that I have said nothing yet about reading and writing—perhaps two of the most important functions in a university man's work. They have been omitted only because there has been no time for them yet on your schedule, though you may be able to devote to this some of the 5 to 7.30 P.M. period, if your research programme and the usual staff committees permit. (The committees will be a bore and an utter waste of time, but you will have to go to reveal your interest in the life of the hospital, to show that you are not aloof and that you feel it to be *your* hospital; otherwise the part-time staff are convinced that you are not of the same flesh and blood.)

The awful truth must be dawning on you: your main work is done after dinner at home every evening until bedtime. I admit that there are some who avoid this and appear able to find leisure in the evening; but they are falling behind in the race. If you wish to keep pace with the journals, if you wish to be a contributor both of your own knowledge and in the many other little ways such as reviewing, annotating, and abstracting, no evening of leisure can be yours. And it will get worse as your contributions achieve recognition, for you will receive requests to write sections of textbooks, then whole works—requests you will have difficulty in refusing. Then your weekends will go. Quite suddenly you will realise that you no longer live like a man, for you don't see your wife, you don't know your children, and you have nothing to look forward to—except toil.

So now you see, my boy, why I commiserate. But there is something greater than your personal future at stake, and you will doubtless have observed what it is. Lost in that morass is the scholar we had hoped for; he's turned into a hack. And this is the problem that you have to face and solve—how to achieve the task set by the Goodenough Committee without killing the germ it intended to nurture—how to deflect the trend of the last decade and achieve leisure. For without being assured of leisure—leisure to read, paint, compose, garden, even doze if you will—your ideas will remain unborn and your inspiration will wither. So good luck, my boy.

PS.—And don't forget you came up the easy way!

YOURS,

P. G.

## Public Health

### Windscale and After

THE accident at Windscale no. 1 pile on Oct. 10 took place during a controlled release of stored Wigner energy from the graphite of the pile. In a reactor of the Windscale type uranium bars sealed in metal cans are arranged in channels through a block of graphite, 50 ft. high and 25 ft. thick. The graphite slows down the neutrons emitted during nuclear fission so that the chain reaction can take place. Some of the neutrons' energy becomes stored in the graphite and is known as Wigner energy. It must be dispersed from time to time under controlled conditions in what is called a Wigner release; and to do this the graphite is heated above the temperature normal for everyday operation. The Wigner energy is then dissipated as heat and the reactor can go back to its normal routine. Eight such releases had been carried out in the no. 1 pile up to the end of 1956, and the procedure followed was to shut down the pile, arrange the appropriate instrumentation, and then cause the pile to diverge with no coolant airflow. The uranium and graphite temperatures then rose and the Wigner release began in the graphite and was self-sustaining. On three occasions it had been found necessary to apply a second nuclear heating because it seemed that the release of Wigner energy was coming to a halt before all the graphite had been annealed. Such a reheating was judged to be necessary on Oct. 8, and the committee of inquiry into the accident concluded[1] that the immediate cause of the trouble was the application too soon and too quickly of this second nuclear heating. The too-rapid rise in temperature led to the failure of one or more cartridges in the pile, whose contents then oxidised slowly, eventually leading to the fire detected on Oct. 10.

The committee refer to two separate and distinct faults of instrumentation affecting the second nuclear heating. First, the uranium thermocouples were situated at the region of highest uranium temperatures during normal operations and were not at the position of maximum uranium temperatures during Wigner release. Thus, the pile operator did not know that the uranium fuel in the middle front regions of the pile was probably hotter than was indicated by the readings he was taking. Second, the pile power meter, though correct for normal operations, read low in the situation prevailing.

The Medical Research Council appointed an independent committee, under the chairmanship of Sir Harold Himsworth, to examine the health and safety aspects of the accident and to comment on the report of Sir William Penney's committee of inquiry. Their findings are included in the Whitepaper[1] published last week.

*Protection of Windscale Workers*

The maximum air contamination within the works occurred from about midnight on Oct. 10 to noon on Oct. 11. Examinations made at that time showed that the radioactivity was almost entirely due to $^{131}I$. The M.R.C. committee were satisfied that no worker could have inhaled a harmful amount of $^{131}I$; and they were also satisfied that no harmful amounts of plutonium or any other element were released.

1. Accident at Windscale No. 1 Pile on 10th October, 1957. Cmd. 302. H.M. Stationery Office. Pp. 27, 1*s.* 3*d.*

Records for total-body irradiation, as measured by film badges worn by Windscale workers, were available for the thirteen weeks up to Oct. 24. 14 persons concerned in the accident had exposures of more than the permissible limit of 3·0r in those thirteen weeks; the highest figure was 4·66r. The committee say: "Normally exposure is only a small fraction of this [3·0r]. Should, however, 3.0r be exceeded by a small amount, as in the highest exposure recorded here, then, provided those exposed are removed from contact with radiation for the requisite period, it can be assumed that no ill effects of any sort will follow."

Among Windscale workers, the highest level of radio-iodine measured in the thyroid gland was 0·5 μc. This amount of $^{131}I$, the committee add, will cause no harm and there is no evidence of significant exposure to any other radio-isotope of iodine. Measurements of radio-strontium in the urine were available for the 30 workers judged to be among the most exposed. From these it has been calculated that the total amount of radiostrontium taken into the body cannot, for $^{89}Sr$, be more than a hundredth of that which could be accepted as a sustained level, and for $^{90}Sr$ it was an even lower proportion of what could be accepted.

In the course of emergency operations some workers looked for a short time through open plug holes into the pile, and the committee considered whether in so doing they might have been exposed to neutrons, which can damage the eyes; but there was no possibility of any significant flux of neutrons being present when the men looked into the holes nearly forty-eight hours after the nuclear heating was stopped.

*Protection of the Public*

The committee agree that the health-physics manager at Windscale correctly assessed the situation in deciding that inhalation and external irradiation were likely to prove well within acceptable limits and that the main problem might arise from ingestion of contaminated food. The one food of importance in relation to the accident was cow's milk, since radioactive materials deposited on grass over a wide area may be collected by grazing cows and excreted in the milk in a high concentration.

The committee concluded that, for both isotopes of strontium, the highest levels in locally produced milk were well below those at which an appreciable hazard would arise were such milk to be consumed over a period of years. "Although it seems most unlikely that any further increase in contamination of the grass will now occur, we feel that a close watch needs to be kept on the radiostrontium levels in milk so that ample warning may be obtained of any upward trend." Contamination with radioactive caesium had also been negligible, which was important because otherwise this isotope might have caused a genetic hazard.

The isotope which rightly received most attention was $^{131}I$. Although a tolerance level had been agreed to for water contamination, no figure for milk had been formally fixed. After consultation with other experts, those responsible at Windscale decided that milk containing more than 0·1 μc of $^{131}I$ per litre should not be consumed by human beings. The M.R.C. committee calculated the maximum amount of $^{131}I$ that a child in the control area might have received in the longest period that elapsed before uncontaminated milk was brought in from outside. This greatest risk was not regarded as in any way likely to be serious; and the committee felt, therefore, that they could justifiably say that it was in the highest degree unlikely that any harm had been done to the health of anybody in the course of this incident.

"Lastly," the M.R.C. committee ends its report, "we feel it only right to pay tribute to those who had to take the responsibility for the health and safety of the population in and around Windscale. They were faced with a new situation and this revealed some defects in organisation and emphasised gaps in our scientific knowledge. But the measures they took and the improvisations they devised were essentially right, and once these were brought fully into play, they were applied decisively and to good effect."

*Further Evaluation*

In a memorandum in the whitepaper, Sir Edwin Plowden, chairman of the United Kingdom Atomic Energy Authority, said that the Authority accepted full responsibility for the accident and regretted the disturbance and anxiety caused to so many people. The cause of the accident lay partly in inadequacies of instrumentation and partly in faults of judgment by the operating staff. These faults of judgment were themselves attributable to weaknesses of organisation. The Authority had already taken immediate measures to deal with organisational weaknesses pending a more comprehensive evaluation of the remedies required. The Authority suggested to the Prime Minister that he appoint some independent person of standing to undertake this evaluation and to recommend what technical and organisational improvements were needed. The accident, Sir Edwin continued, had indicated the need for closer liaison between the management of the factory and various local interests. A standing liaison committee had, therefore, been set up at Windscale, and similar committees were in process of being set up at all other operating factories of the industrial group of the Authority.

Following Sir Edwin's suggestion, the Prime Minister asked Sir Alexander Fleck, chairman of Imperial Chemical Industries Ltd., to recommend what measures were needed to remedy the deficiencies. Sir Alexander had agreed to do this, and three committees have been formed under his chairmanship, dealing respectively with technical evaluation, organisation, and health and safety.

In the House of Commons last week, Mr. Macmillan gave assurance that the Windscale accident had no bearing on the safety of the nuclear power stations being built for the Electricity Authorities (for reasons of construction set out in the whitepaper). He said he would carefully consider the question of publishing the reports of the Fleck committees.

## Influenza

In the week ended Nov. 2, in the 160 great towns of England and Wales 263 (396) people were certified as having died from influenza, 404 (505) from pneumonia, and 315 (478) from bronchitis (previous week's figures in parentheses). The number of new claims on the Ministry of Pensions and National Insurance in England, Wales and Scotland fell by nearly 100,000 to 299,302 in the week ended Oct. 29—still nearly twice the number for the corresponding week of 1956.

According to the World Health Organisation, the epidemic has passed its peak in many parts of Europe and the United States. There was some recurrence in Turkey and in Japan and other Asiatic countries when children returned to school after the summer holidays.

## Future of Mass Radiography

A Ministry of Health memorandum [1] to regional hospital boards says that the decline in the prevalence of tuberculosis requires that mass-miniature radiography should be more selective. The proportion of active cases found has been much higher among general practitioners' referrals than among the general public, particularly in men aged 55–64; and in them the prevalence of cancer is almost as high as that of tuberculosis. But radiography of schoolchildren yields so poor a return that it is justifiable only for contacts or those found to be tuberculin-positive.

Thus the need for more services is largely a need for more static units. These are best sited at hospitals because this makes coordination with other specialties easier—a particularly important point now that so many of the lesions found are not tuberculous. The Ministry has lately bought six 100 mm. cameras, which are expected to prove very suitable for this work and to avoid the use of many large films. Mobile units, the memorandum adds, should direct most of their attention to people in whom the prevalence of tuberculosis is likely to be high or the risk of spread great—e.g., those in poor, overcrowded areas, older men, teachers and others dealing with children, food-handlers, vagrants, and tuberculin-positive children. The use of 70 mm. cameras, and central processing of films, should lead to more accuracy. Light mobile units, equipped only for radiography, would be suitable for rural areas.

1. H.M. (57) 94.

## Lonely Old People

In his presidential address to the Society of Medical Officers of Health, Dr. H. D. Chalke [1] said that the number of old people living alone had doubled in the past twenty-five years, and that many hospital beds were occupied by the single, widowed, or divorced. Dr. D. Warren Browne, medical officer of health for Chichester, points out in his report for 1956 that, with the reduction in the size of families over the past fifty years, many of the old people of 1970 will be "only children of only children," without brothers or sisters, nephews or nieces. He says that it is one of the saddest of his duties to move old people against their wishes to institutions. "The rapidity with which some of them die, for no reason other than a loss of desire to continue to live once they are removed from their homes and belongings, however squalid these homes may have become, is a matter of deepest concern for all of us." Old people's homes, he says, are unlikely to be opened quickly enough to keep pace with the increasing number of old folk needing help; he hopes for a "realistic housing policy" to enable them to live their last few years surrounded by their own belongings in circumstances where a watchful eye can be kept on them.

## Statistics of Incapacity

The Ministry of Pensions and National Insurance has issued another in its series [2] of collections of statistics about sickness and injury in the working population.[3] One appendix helps in the interpretation of figures—e.g., it points out that the figures are incomplete in that they exclude people ill for less than four days and people ineligible for benefit. Another gives further sources of information about sickness and injury benefits. The tables are in three parts, concerned severally with sickness benefit, injury benefit, and the population at risk, and deal chiefly with the period June, 1954, to June, 1955.

## The Registrar General's Weekly Return

Beginning with the return for the week ending Feb. 1, 1958, the Registrar General's weekly returns will no longer give the totals for the 160 great towns in England and Wales. Instead, table I will give figures for (*a*) London administrative county and (*b*) England and Wales. At first, precise aggregates for previous years will not be available, but approximate cumulative totals will be given. Table II will show the figures for England and Wales, for each county, and for the English boroughs with populations over 500,000 (Birmingham, Leeds, Liverpool, Manchester, and Sheffield) and for the four largest Scottish and Irish cities (Edinburgh, Glasgow, Belfast, and Dublin).

1. Chalke, H. D. *Publ. Hlth*, 1957, 71, 283.
2. See *Lancet*, 1955, ii, 1142.
3. Ministry of Pensions and National Insurance, Digest of Statistics Analysing Certificates of Incapacity, 1954–55.

## Infectious Diseases in England and Wales

| Disease | Week ended October | | | |
|---|---|---|---|---|
| | 5 | 12 | 19 | 26* |
| Diphtheria | 3 | 1 | 1 | 3 |
| Dysentery | 265 | 210 | 175 | 197 |
| Encephalitis: | | | | |
| Infective | 3 | 13 | 3 | 2 |
| Post-infectious | 7 | 4 | 4 | 6 |
| Food-poisoning | 115 | 106 | 90 | 108 |
| Measles, excluding rubella | 1329 | 1218 | 1310 | 1414 |
| Meningococcal infection | 14 | 38 | 31 | 35 |
| Ophthalmia neonatorum | 34 | 24 | 26 | 35 |
| Paratyphoid fever | 4 | 5 | 7 | 1 |
| Pneumonia, primary or influenzal | 1882 | 2278 | 2281 | 1897 |
| Poliomyelitis: | | | | |
| Paralytic | 88 | 68 | 64 | 56 |
| Non-paralytic | 29 | 26 | 16 | 10 |
| Puerperal pyrexia | 271 | 354 | 307 | 287 |
| Scarlet fever | 306 | 336 | 382 | 399 |
| Smallpox | — | — | — | — |
| Tuberculosis: | | | | |
| Respiratory | 440 | 494 | 529 | 515 |
| Meninges and C.N.S. | 8 | 2 | 5 | 6 |
| Other | 49 | 60 | 52 | 68 |
| Typhoid fever | 6 | 5 | 2 | 4 |
| Whooping-cough | 383 | 317 | 318 | 349 |

* Not including late returns.

# In England Now

*A Running Commentary by Peripatetic Correspondents*

An interest in medical history is said to be a sign that a physician has become middle-aged or worse. Those of us thus afflicted can perhaps take comfort in the fact that Osler, when 65, wrote:

"Completed today 10 years in Oxford. I have not done much in the profession here but I have done 3 useful things, or better, helped to. (1) The Assoc. of Brit. Ph. (2) The Quarterly Journal of Medicine. (3) The Historical Section of the Roy. Soc. Med."

Osler took a great interest in medical geography, as any student of his textbook will testify; and he would have been greatly pleased, I fancy, to know that in East Africa a four-year-old Association of Physicians is prospering. Its members—all of them fellows or members of one of the Royal Colleges of Physicians—often have to travel hundreds of miles to their meeting. (From Dar-es-Salaam to Kampala, where this year's meeting was held, is a thousand as the aeroplane flies.) Its objects are like those of the American and British Associations of Physicians—to advance knowledge of internal medicine and to promote friendship among physicians.

Occasionally I think that I spend too much time at medical meetings; but this one opened my eyes wider—to the canopy of the forest harbouring mosquitoes different from those at ground level, to birds suspected of being the reservoirs of viruses, to tropical diseases in abundance, and to temperate diseases in new guises.

I was the happy bearer of a message of good will from the president of the Association of Physicians of our country and from the Royal College of Physicians of London. At the president's sundowner—an appropriate word on the Equator where the sun ends its orbit within half an hour of 6.30 throughout the year—I met friends I had not seen for years; and incidentally I learned for the first time that being up a gum-tree is a delicate position because its long trunk has no branches for descent.

* * *

The world is full of those who decry everything that is English. Our weather is too cold, our climate too damp. The taxes are too high, the buildings are not high enough. Our buses are too full, our lives too empty; our shops too dull, our pageantry too flashy; our clothes too woolly and our mutton too tough; our sportsmen never win and our strikers never work; our eggs are too old, our music too modern; our politicians too many and our children too few. Yet despite my life-long familiarity with these national discrepancies, I must confess that my first impression of the United States was of sheer topsy-turvy lopsidedness. Everything seems crazy—the buildings, the cars, the language, the dollar. My New York hotel was like a city unto itself, with its 24 floors, its 2000 rooms, its shops, its own cinema, and a foyer as big as Waterloo Station. My bill for the night came to 12 dollars, but then the dollar is crazy—you get 3 for £1 and spend them like half-crowns.

The language takes some getting used to: not only is it incomprehensible to me, but the Queen's English is often incomprehensible to the inhabitants. Fortunately this is no bar to the establishment of familiarity. The professor is Sam, my other chief Joe, the intern Bob (pronounced Bub), and I am Herb. After all, we have known each other two days.

On my second day, Joe insisted I had dinner at his house. We started out from the hospital car-park. Joe had some hard things to say about its inadequacy. (Given half a dozen parks of similar size in central London, parking would cease to be a problem.) Tentatively, I asked him whether some of his difficulty was not due to the size of his car. With massive bumpers, an elongated bonnet, three rows of seats each wide enough for four to sit in comfort, and an enormous boot, it looked more at home at a bus-stop than in a car-park. His reason for running such an outsize vehicle was illuminating. On an outing with his three children and three dogs (plus the not infrequent addition of friends for both children and dogs), he finds himself, if anything, short of room; and, since peace en route varies in direct proportion to the distance between any two of his children and/or dogs, he

often finds it preferable to take half the family in his car while his wife follows with the other half in her own car.

* * *

Having at last attained the coveted position of senior registrar, the next problem is where to go at the end of the four years. One's first thought is naturally that great Western country where many of one's predecessors are installed among the lakes and maple trees. As winter draws on, the attraction of warmer climates becomes more insistent; old *Lancets* are opened to see whether medical officers are often required in the Gilbert Islands; letters are sent off to the Governments of Borneo and Ceylon; and pamphlets on one's desk proclaim *A New Life in the Rhodesias*.

But now that the rain is pouring down and the children are at last in bed, we had better get down to that world-shattering paper which is surely going to earn us a geriatric consultancy in outer suburbia.

* * *

In one of our wild moments a few months ago we bought a refrigerator. Not one of these massive jobs we have seen in the houses of our clinical colleagues, with automatic defrosting at 3.20 A.M. and a special compartment for caviar; just a small affair to keep our milk cool. For some time after it came we used to open and close the door happily, watching the light come on, but after a while we came to accept cold milk as one of the facts of life, and even acquired a taste for hard butter. Judge, then, of our dismay when the other day the refrigerator packed up and refused to work for us any more. Our sunny disposition became quite clouded, and we spoke snappily to our youngest child. Clearly something had to be done, and our scientific training led us at once to the solution; we rang up the refrigerator chap.

He was not surprised to hear from us. "I've been expecting this to happen," he said, in a manner reminiscent of surgical outpatients. "Listen," said the chap, "there's only one thing to do. Switch her off and let her cool. Turn her upside down and you'll hear her gurgle. Let her sit for about half-an-hour and then turn her back again. There's a 75–90% chance you'll get good function again; but if not," said the refrigerator chap briskly, "you can't expect any function at all."

We are not very quick on the telephone, and clinical instructions always did confuse us, but eventually the position got across, and we ventured to ask what happened if we got no function. "Ah," said the chap with some unction, "new unit; nineteen pounds six and eleven."

We turned her upside down with considerable trepidation, which rapidly changed to black despair when we found she did not gurgle at all. She sat for half an hour in an atmosphere of mounting tension, and when we went back to turn her again we observed to our horror a sullen stream of yellowish sticky fluid emanating from her mechanism. Greatly daring, we inserted an exploratory finger and traced this to its source—a sodden handkerchief containing a quantity of boiled sweets deposited there for safety by our youngest child. We called for our toothed dissecting forceps and disimpacted the offending mass. Immediately our ears were gladdened by a reverberating gurgle of a singularly musical quality. She gurgled contentedly for nearly five minutes and then relaxed into a placid stupor. Confidently we turned her over; we switched her on and off she went. She has given us good function ever since, and we are thinking of inviting our clinical colleagues to an ice-cream conversazione.

* * *

THE OBSTETRICIAN'S WEEK

Monday's child is brow or face,
Tuesday's child is one of a brace,
Wednesday's child needs turning and heaving,
Thursday's child is the better for leaving,
Friday's child is distressed and blue,
Saturday's child goes breech-wise through,
But the child that's born on the Sabbath day
Is a first or second stage delay,
Or else the placenta decides to stay,
Or the cord gets tangled and goes astray,
Or something or other gets in the way,
But even if it's just a B.B.A.
And there's only a perineum to mend,
It effectively ruins the whole weekend.

# Letters to the Editor

## EPSOM COLLEGE

SIR,—You were good enough to draw attention[1] to the needs of Epsom College for many improvements and to the appeal to the profession for the money necessary to carry them out. Progress was reported in an interim statement,[2] which you also kindly published; and it is now due to subscribers that they be informed of the present position. If all those who have signed covenants survive for the full seven years, we have in sight a net total of about £60,000. This includes several bequests, allocated to this fund by the council, which would, in the ordinary way, have gone to swell the endowment. It includes also generous assistance from the British Medical Association and the Medical Insurance Agency. The balance, subscribed by members of the profession and by Old Epsomians, many of whom are doctors, accounts for less than £40,000. This result, frankly, is disappointing. The needs of the college are so urgent that the council have already embarked on a new boarding-house and new laboratories and classrooms, and will still be faced with rebuilding the kitchens and dining-hall. These essential projects will cost far more than the appeal has produced, and to meet the cost it will be necessary to use the whole of the endowment-fund and the general-purposes-fund investments, a most regrettable but inevitable expedient.

The centenary fund has not been closed, and we do beg the profession to help. The new buildings are actually going up and are open to inspection at any time. Medical men and women are urged to pay a visit to satisfy themselves of the merits of the planned expenditure. Financially, the college will be hard hit when the improvements have been paid for; but the council have realised that the efficiency of the college is at stake and that their duty has been to go forward with them. We need much more help, and we do urge the 98% of the profession who have not yet responded to the appeal to contribute, whether or not they are already regular subscribers to the charitable funds administered by the college for the benefit of the widows and orphans of medical men.

HENRY ROBINSON
RONALD W. RAVEN.

Epsom College, Surrey.

## INFLUENZAL PNEUMONIA TREATED WITH CORTISONE AND ANTIBIOTICS

SIR,—The letter from Dr. Plaza de los Reyes and his colleagues (Oct. 26) raises the whole question of the role of cortisone and its derivatives in the acute infections. This is a subject which has interested me greatly since I first had experience of their almost magical effects in fulminating meningococcal infections (Waterhouse-Friderichsen syndrome). For several years now I have used either cortisone or prednisone empirically in a number of cases where, despite chemotherapy, the patient's condition was seriously deteriorating, and in no case have I been disappointed. I suggest that our views on these matters must be reconsidered. It is well known that, presented simultaneously with an infectious agent, cortisone, by suppressing the body's reaction, may cause serious harm. Again, in patients long under treatment with cortisone, dangerous suppuration may occur with minimal signs, and fatal results. These facts seem to have led the profession to conclude, in my opinion erroneously, that cortisone in the infections is highly dangerous.

I submit that the position is quite different when once the body defences have been seriously challenged and stimulated to the maximum production of antibodies. I believe that if, in spite of chemotherapy in an acute infection, the patient's condition continues to deterior-

1. *Lancet*, 1954, ii, 1116.
2. *ibid.* 1955, ii, 1041.

ate, cortisone should be tried. After all, we should consider that in many instances it is not the invading organism which kills, but the patient's overemphatic reaction to it. In such circumstances, I believe that cortisone may, by damping down this reaction, give the defences time to come to grips with the invaders. In my experience, cortisone is especially efficient in meningococcal infections, collagen diseases, and glandular fever. But its value is not limited to these conditions. Indeed, I would lay it down as a principle that no patient should be allowed to die from *any* acute infectious process without the exhibition of cortisone. This need not be a lengthy procedure. It should be clear within forty-eight hours whether or not cortisone is likely to be successful. If no change is apparent, then it should be stopped. Should it prove successful, it is my practice to continue it in full doses for roughly a week, and then another three days on half the dose. This should not seriously alter the body's chemistry. Incidentally, I have not found it necessary during the present epidemic to treat more than one influenzal pneumonia with cortisone, and I do not feel that its routine use is either necessary or desirable.

These are merely a few observations on a subject which I am sure has also engaged the attention of many of my colleagues. Perhaps this letter may stimulate them to record their own experiences, and start a discussion which, I feel sure, could be of considerable value.

South Middlesex Hospital, Isleworth, Middlesex. G. E. BREEN.

SIR,—In the absence of bacteriological details, the claim made by Dr. Plaza de los Reyes and his colleagues (Oct. 26)—that cortisone (combined with appropriate antibiotic therapy) exerts a dramatic action in influenzal pneumonia—cannot be accepted at its face value.

Of 100 patients with influenza under my care since Sept. 1, only 14 had pneumonia confirmed by radiological examination; of these 4 died within forty-eight hours of the onset of pneumonia, 2 within twenty-four hours of admission. In these 4 the presenting symptoms were drowsiness, rapidly proceeding to coma (in sharp contrast to the classical manifestations), with severe dehydration in the 4th case from concomitant vomiting and diarrhœa. In these fatal cases sputum was scanty and usually blood-stained. The bacteriological findings were:

Case 1: *Staphylococcus aureus* sensitive to chloramphenicol and erythromycin.

Case 2: *Staph. aureus* sensitive only to erythromycin.

Case 3: Hæmolytic streptococcus sensitive to the common antibiotics and *Staph. aureus* resistant to all the antibiotics tested.

Case 4: Friedländer's bacillus isolated from the gut as well as from the lungs, sensitive in varying degree to the common antibiotics with the exception of penicillin.

Within a few hours of the onset of pneumonia, cortisone or corticotrophin was administered parenterally and continued until death; case 2 received in addition large doses of staphylococcus antitoxin intramuscularly (because of a history of hayfever), while all were given various combinations of antibiotics chosen empirically since the results of the sensitivity tests were not available during life. Chloramphenicol was avoided in 2 of the fatal cases because the leucocyte-count was below 2000 per c.mm. and neutrophils below 50%. All the patients were nursed from the outset in oxygen-tents and given electrolytes and plasma intravenously.

Necropsy revealed extensive pneumonic consolidation, and toxic changes in the myocardium and in the suprarenals, but no hæmorrhages. Case 3 had a pericarditis from which hæmolytic streptococci were grown.

In 2 cases a low blood-pressure rose slightly, but whether this was an advantage remains uncertain. Cortisone was not considered necessary for the 10 patients who recovered, from whom a variety of secondary organisms were isolated—viz., hæmolytic streptococci, *Hæmophilus influenzæ*, and pneumococci, as well as strains of *Staph. aureus* that appeared to lack the lethal properties of those already described. Some means of assessing staphylococcus virulence additional to the coagulase test appears overdue.

To summarise briefly. Virus pneumonia, in its various forms, including influenzal, is a mild disease rarely causing death or permanent damage, although the process of resolution may be accelerated by cortisone or like therapy. On the other hand, secondary bacterial invasion is always potentially dangerous, particularly if more than one microorganism is involved, making antibiotic therapy difficult as access to the pneumonic areas is limited compared with lobar pneumonia. Cortisone therapy, if interfering with the immunity mechanism, may readily tip the scales against the patient in a fulminating attack.

London, N.W.3. WILLIAM GUNN.

## BACTERIA AND INFLUENZA

SIR,—An outbreak of influenza began in Newton-le-Willows in August and has recently ended. It appears to have been similar to those reported in other parts of the country, with a high attack-rate, rather varied clinical picture, low incidence of complications, and tendency to relapse in some people.

Paired samples of blood were collected from six patients whose early symptoms were typical of influenza, but antibodies to influenza Sol A were found in the "convalescent" serum of only three, two of whom had bronchopneumonia, confirmed radiologically. The first was a man, aged 21, from whose sputum was isolated a pure growth of Friedländer's bacillus. He coughed up a good deal of bright-red blood on the second, third, and fourth days and then recovered rapidly. The second was a woman, aged 42, whose sputum contained a mixed growth of organisms, *Neisseria catarrhalis* predominating.

Bronchopneumonia was very uncommon here, and neither *Staphylococcus aureus* nor *Hæmophilus influenzæ* were isolated from the few sputa that were examined. There were no deaths.

If any inference may be drawn from so small a group of investigated cases it must be the disagreeable one that the diagnosis of influenza was mistaken in probably half of the large number of instances in which it was made. More astute physicians than I will do better than this, but not so much better that they can, from clinical observation alone, draw valid conclusions about any particular outbreak of influenza in the general community. If the influenza virus is not to be made whipping-boy for a variety of other agents, such observations must be backed up by ætiological investigation.

Newton-le-Willows, Lancashire. W. H. LYLE.

## UNILATERAL "EMPHYSEMA"

SIR,—During the past few years at the London Chest Hospital we have come to regard "unilateral emphysema" as a not uncommon condition. This is perhaps due to our special interest in this subject.

After excluding the obvious causes—bronchiectasis and bullous cysts—we have come to the conclusion that most cases are due rather to anomalies of the pulmonary arteries than to primary pulmonary abnormality.

The anomalies may take the form of hypoplasia of a whole pulmonary artery, as in the case described by Smart and Pattinson,[1] or hypoplasia of a lobar artery, as in three cases described by Belcher and Pattinson.[2] We believe that the lesion is congenital and that the pulmonary abnormalities are secondary to it.

The syndrome consists essentially of an unusually translucent lung or lobe which occupies less space than

1. Smart, J. Pattinson, J. N. *Brit. med. J.* 1956, i, 491.
2. Belcher, J. R., Pattinson, J. N. *J. thorac. Surg.* 1957, 34, 357.

it might normally be expected to do. Where we have seen this the prediction that hypoplastic arteries are present has frequently been confirmed by angiography. Dr. Dornhorst and his colleagues (Nov. 2) stress the fact that the hilar shadows were small in their cases, and we feel sure that had angiograms been done hypoplasia of the whole or part of the pulmonary arteries would have been demonstrated. The fact that the oxygen uptake was so small strongly suggests that a whole rather than a lobar artery was involved.

We feel that the term "unilateral emphysema" is misleading in these cases as no emphysema may be present. Hypoplasia of the pulmonary or lobar artery is, we think, a better term.

J. R. BELCHER
J. SMART
J. N. PATTINSON.

The London Chest Hospital, London, E.2

## VALUE OF AEROSOL TRYPSIN

SIR,—Your editorial on expectorants (Nov. 2) concludes that trypsin acts only as a water mist, is too irritant, and produces a dangerous metaplasia.

The argument has been effectively confused by the introduction of theoretical considerations and the suppression of clinical evidence. Furthermore, a number of very different clinical states have been considered at once: chronic secondarily infected tuberculosis and bronchiectasis, chronic bronchitis, and acute bronchitis in patients with an otherwise normal bronchial tree.

Our article of Oct. 26 reported results in the last group only, with special reference to the prevention and treatment of atelectasis. We are concerned lest the value of the treatment to this group may be missed as a result of selective quotation applied out of context.

No mention was made of work clearly showing that aerosol trypsin produced better results than a water mist. Camarata et al.[1], in a study of 104 patients, paralysed like our own, compared the effects of a water mist containing trypsin with a water mist containing 'Triton A.20.' On your argument there should have been no difference between the results. They state, however:

> "Of the 88 patients treated with 'tryptar' there was only one failure. . . . There were actually 16 patients treated with 'triton A-20' but as stated above there were nine failures who were then treated with 'tryptar' and cleared completely under this treatment. It can readily be seen that tryptar is the most successful agent. 'Triton A-20' was less than 50 per cent. effective in clearing atelectasis, where 'tryptar' was more than 95 per cent. successful. When comparing 'triton A-20' and 'tryptar' as to length of time necessary for complete clearing, 'tryptar' was successful in clearing 68 per cent. of the acute cases and 42 per cent. of the chronic cases in two weeks. 'Triton A-20' cleared only 14 per cent. of the acute cases and none of the chronic cases in two weeks."

Our own results with trypsin approximate in success-rate to Camarata's trypsin series, whereas without aerosol treatment there were several failures and 2 deaths.

Palmer,[2] whom you quote in support of the view that aerosols act only as water mists, was treating patients with chronic bronchitis who had permanent sputum, and in any case found it necessary to give 60 ml. of inhalation per diem. In our type of patients, different from Palmer's, we have noted loosening of sputum after the inhalation of as little as 0.5 ml. in five minutes; scarcely dilution!

You cite Limber et al.[3] as support for your statement that trypsin gives rise to "side-reactions, including dyspnœa, fever, hoarseness, and nasal and eyelid irritation." But a footnote to their article states "with highly purified trypsin available at present hoarseness and mucosal irritation have not been observed following the last 50 treatments." This you did not mention. Forbes and Wise,[4] whom you also quote in support, did not apparently use an adequate baffle to trap large droplets, nor did Farber et al.[5], to whom you also refer. Limber et al.[3], Habeeb et al.[6], Camarata et al.[1], and ourselves, on an experience with over 300 patients and over 12,000 administrations of trypsin, agree that with modern purified trypsin and an adequate baffle, side reactions are completely unimportant. The chests of quite a number of our patients became "dry" while still receiving aerosol trypsin, which again hardly suggests irritation.

You quote Farber et al.[7] as having found atypical metaplasia and dyskeratosis in the sputum of patients six months after the cessation of administration of trypsin. To check this finding, Habeeb et al. examined 30 similar controls and 30 similar patients before, during, and after thirty days' treatment with trypsin and found no evidence of any "peculiar cellular change" or "metaplasia" which is not already known to be a "feature of the pathologic picture of *the disease*" (our italics). The patients compared from this point of view had all permanent sputum as a result of *tuberculosis*. Once again the argument in your leader is bedevilled by the mistaken application of apparent findings in one group of patients to a treatment proposed for an entirely different group.

Your conclusions, Sir, ignored facts which were available, and if taken at face value will deny to many patients the benefit of a therapy which might well have proved lifesaving.

A. B. KINNIER WILSON
F. HARWOOD STEVENSON.

Institute of Orthopædics, Royal National Orthopædic Hospital, Stanmore, Middlesex.

## INTERNATIONAL MEETINGS

SIR,—When I recently returned from, I believe, the eighth international congress which I had attended, I felt that by now I had learnt how not to organise and run a congress. Your leading article last week made me wonder whether anybody would be interested in my views.

I start from the premise that one does not attend such a congress, in your words, "in the serious hope of acquiring new knowledge." You quote a number of incentives, from finding out whether "X and Y were as big liars" as they were judged to be from their published papers, to "merrymaking in a foreign climate," so the most important point is the meeting or at least seeing colleagues who work in the same field as oneself. It is, therefore, necessary that those one meets and oneself should have a language in common, and in my opinion it serves no useful purpose to go to one of these gatherings if one's native language is one's only linguistic equipment. Once this is admitted there is no need for the elaborate arrangements of simultaneous translations into the various languages, nor must we suffer from the *soi-disant* bilingualist.

The next thing to be avoided is the parallel sessions. They cause one to chase from auditorium A to lecture-theatre B, only to find that lecturer X had to cancel his lecture and therefore Y, whom we wanted to hear, has already finished his paper and we now have to listen to that old bore Z again.

The formal sessions should occupy only half of the day; the other half can be used for visiting the institutes, hospitals, laboratories, picture galleries, bull-fights, operas, cricket matches, and particularly one's friends, old and new. The holding of spontaneous symposia by interested people should not be forbidden.

1. Camarata, S. J., Jacobs, H. J., Affeldt, J. E. *Dis. Chest*, 1956, **29**, 388.
2. Palmer, K. N. V. *Lancet*, 1957, **i**, 611.
3. Limber, C. R., Reiser, H. G., Roettig, L. C., Curtiss, G. M. *J. Amer. med. Ass.* 1952, **149**, 816.
4. Forbes, J., Wise, L. *Lancet*, Oct. 19, 1957, p. 767.
5. Farber, S. M., Gorman, R. D., Wood, D. A., Grimes, O. F., Pharr, S. L. *J. thorac. Surg.* 1954, **27**, 45.
6. Habeeb, W., Reisser, H. G., Roettig, L. C., Curtis, G. M. *Dis. Chest*, 1954, **26**, 408.
7. Farber, S. M., Pharr, S. L., Trant, H. F., Wood, D. A., Gorman, R. D. *Lab. Invest.* 1954, **3**, 33.

I realise that this requires ruthless elimination of many papers, but can anybody think that a bad thing who has studied programmes of congresses? Only too often does it seem as if papers are read because the organising committee wished to be courteous to a country and not exclude its speaker or speakers, although their contribution may be minimal.

I hope that steps like these may reduce the number of people attending a congress; and who except statisticians of congresses or hotel-keepers would regard this as a bad thing?

St. John's Hospital, Stone, Aylesbury. S. L. LAST.

## l-NORADRENALINE IN MYOCARDIAL INFARCTION

SIR,—A study of the effects on the electrocardiogram of l-noradrenaline in hypotensive oligæmia in the dog, shortly to be published, confirms the findings of Dr. Littler and Dr. McKendrick (Oct. 26). The overall survival-rate of dogs made oligæmic and hypotensive is not improved by elevation of blood-pressure with l-noradrenaline, as compared with untreated control animals[1]; the time of their deaths, however, is different—treated animals often dying with heart-block or ventricular fibrillation during actual administration of the drug. Atropine might, as Professor Maegraith (Nov. 2) suggests, lead to significant improvement in similar circumstances.

Unfortunately, it has been found that, in experimental oligæmic hypotension, the gross abnormality in cardiac carbohydrate metabolism is not reversed towards normal by l-noradrenaline as it is by blood-transfusion. Furthermore, l-noradrenaline in the heparinised hypotensive dog regularly leads to extensive subendocardial hæmorrhages.

Knowing the great capacity of vital organs to increase their extraction of essential metabolites from the reduced volume of blood reaching them in shock states, one wonders whether patients with hypotension who are given l-noradrenaline and recover do so in spite of this therapy and not because of it.

University Department of Surgery, The Royal Infirmary, Sheffield. B. N. CATCHPOLE.

## OVER THE HILLS FROM WINDSCALE

SIR,—After reading the article by Dr. Madge (Nov. 9) one is left wondering how much of it is directed towards restoring the loss of public confidence he deplores.

Much has been made of lack of cooperation between the United Kingdom Atomic Energy Authority and the public-health authorities. As medical officer of the district in which the Windscale incident occurred, I can say quite firmly that this hare was not started in Cumberland. From the outset the county medical officer and myself were constantly in touch with the Atomic Energy Authority and the ministerial and regional representatives of the Ministry of Agriculture, Fisheries and Food, who were promptly on the scene.

I believe I am not the first to suggest that the "grave disquiet" referred to was inversely proportional to proximity to the reactor. Locally the event was simply a sensation, and the population was spared the panic which might well follow the advocated use of warning sirens. Radioactivity in the area never approached a level at which people might have been advised to take protective measures for themselves. Data in support of this were made available at Windscale, and it is difficult to reconcile with this the implication that information was hard to come by.

That information of course was basic material on which any doctor with a fair knowledge of radioactive hazards could form a reasonable judgment. One now has to ask if access to highly technical detail, which is presumably what Dr. Madge desires, is of material value to medical officers of health. Most would be loth, on the basis of their own interpretation of such esoteric facts, to advise any action contrary to the readily available advice of the Ministry of Health, Medical Research Council, and Atomic Energy Authority. We are, after all, accustomed to relying on much expert advice and information. Is it going to become necessary for doctors to verify by personally conducted investigation the safety, for example, of poliomyelitis vaccine?

To tangle risks to unborn generations with a reported high incidence of congenital malformants in South Westmorland is surely treading shaky ground. Till congenital malformations and their causes, where known, are made notifiable there will remain notable gaps in our statistical knowledge.

When, in time to come, the whole affair can be viewed in perspective it is more likely that the invisible vapour from the Windscale chimney will be found to have caused no ill health other than a minor degree of neurosis in the few. Meanwhile the nation daily regards with unwonted complacency the emissions from our industrial stacks, visible reminders of a staggering morbidity due simply to good old-fashioned smoke. Is not the situation Gilbertian?

Whitehaven, Cumberland. J. N. DOBSON
Medical officer of health, Ennerdale Rural District Council.

## "MUNCHAUSEN'S SYNDROME"

SIR,—We should like to report another case of the so-called Munchausen's syndrome.

A woman in her thirties goes under the name of Joyce A. She is about 4 ft. 8 in. tall and very obese, weighing over sixteen stone. She gives a history of having tuberculous peritonitis in 1942, for which she was drained via a laparotomy nine times in Colchester Military Hospital. She says that she is married but separated from her husband, and that she has no children. Her complaint is either of renal colic or of diffuse abdominal pain, mimicking obstruction. She is apt to request pethidine, and when this is withheld she discharges herself from hospital.

We understand that in the past week she has gone through four hospitals in North-West London, and we are drawing attention to her in the hope that she will be recognised in the casualty department, and not needlessly admitted to hospital.

Whittington Hospital, London, N.19. B. H. BASS
M. G. SELSON.

## UNNECESSARY INVESTIGATIONS

SIR—Your peripatetic correspondent (Nov. 2) treats in a jocular manner what has become one of the more pressing and depressing problems of our hospital service—the ordering of unnecessary investigations. He realises that some of the pathological investigations he orders are of no value, but has he considered how many useless X-ray examinations are requested? Does the average pneumonia need to be radiographed more often than once for diagnosis and a second time at an outpatient-department follow-up six weeks later? Has it not been shown that once the duodenal cap is deformed further barium meals are of no value unless a fresh lesion is suspected as well as the chronic duodenal ulcer? Why are barium enemas done before sigmoidoscopy? The preparation is unpleasant for the patient and may take the nurse 1–2 hours. Is any useful purpose served by radiographs of the lumbar spine in the vast numbers of cases of occasional recurrent low-back pain?

This list could be considerably extended. If only those X-rays which are clinically justified were ordered, there would be less difficulty in X-ray departments, most of which nowadays are understaffed; and unnecessary radiation, which we are told may be dangerous, would be avoided.

London, N.19. G. OSBORNE.

1. Catchpole, B. N., Hackel, D. B., Simeone, F. A. *Ann. Surg.* 1955, 142, 372.

## EARLY ADMISSION TO HOSPITAL OF MENTALLY DEFECTIVE BABIES

SIR,—Constructive criticism of medical methods from people outside the profession itself is a useful feature of your correspondence columns. Miss Adams, writing last week about the difficult question of the care of young mentally defective children, has certainly pricked the pædiatrician where it hurts. In describing how the news that he had a mongol baby was broken to a father she says: "The diagnosis was confirmed, but by a pædiatrician rather than a consultant specially qualified in mental deficiency." She goes on to imply that the latter would have made a much better job of it.

Are pædiatricians then really soulless scientists with no appreciation of the emotional and social aspects of the situation?

Surely "consultants in mental deficiency" alone are so few that one would hardly ever be available at the time and place required. The pædiatrician is, or should be, the very one who is most suited to be such consultant, though he may call on the help of others to obtain a clear picture of the problem. I would say that most of us fully understand the fact that diagnosis is not enough, and that in some way we must try to give continued support and advice to the parents. This should mean more than occasional words of encouragement in an outpatient department, and it is in this direction that there is a great need for more organised assistance.

Dorchester. DAVID VULLIAMY.

## IMPORTANCE OF THE ILEUM IN THE ABSORPTION OF VITAMIN $B_{12}$

SIR,—Patients who have anatomical lesions of the small intestine may develop megaloblastic anæmia. Such lesions may be intestinal strictures [1] blind loops and anastomoses,[2] or multiple diverticula of the small intestine.[3 4] The anæmia in these patients is usually due to deficiency of vitamin $B_{12}$ and is thought to be caused by the growth of an abnormal bacterial flora in the stagnant loops of intestine which in some way interferes with the absorption of vitamin $B_{12}$.

Using radioactive $B_{12}$ several groups of workers have in fact demonstrated that patients with the "blind-loop" syndrome are unable to absorb normal amounts of $B_{12}$. Absorption increases to normal in some patients after a course of antibiotics[3 5]; but in others no improvement follows.[6 7] In a series of such patients treated by us with antibiotics the absorption of vitamin $B_{12}$ increased to normal in eight of them. These particular patients suffered from intestinal stricture, diverticulosis, or entero-entero anastomoses; in all, the ileum was present. On the other hand, there was no improvement in absorption in seven patients whose ileum had either been resected or short-circuited by an ileo-transverse anastomosis.

These observations are in keeping with experimental data in the rat, which indicate that vitamin $B_{12}$ is *not* absorbed in the proximal small intestine,[8 9] and with direct observations in man carried out when the small intestine is explored at laparotomy.[10]

It is well known that patients who have undergone total gastrectomy or who have uncorrectable blind loops or intestinal strictures should either be treated with vitamin $B_{12}$ or be kept under regular hæmatological supervision. It would also appear that patients who have had operations which involve removal or shortcircuiting of the ileum should be treated similarly.

Postgraduate Medical School, London, W.12. C. C. BOOTH
D. L. MOLLIN.

1. Faber, K. I. *Hospitaltidende* 1895, **4**, roekke 3, bind 601.
2. Little, W. D., Zerfas, L. G., Trusler, H. M. *J. Amer. med. Ass.* 1929, **93**, 1290.
3. Badenoch, J., Bedford, P. D., Evans, J. R. *Quart. J. Med.* 1955, **24**, 321.
4. Dick, A. P. *Brit. med. J.* 1955, i, 145.
5. Halsted, J. A., Lewis, P. M., Gasster, M. *Amer. J. Med.* 1956, **20**, 42.
6. Doscherholmen, A., Hagen, P. S. *J. Lab. clin. Med.* 1954, **44**, 790.
7. Mollin, D. L., Booth, C. C., Baker, S. J. *Brit. J. Hæmat.* 1957, **3**, 412.
8. Booth, C. C., Chanarin, I., Anderson, B. B., Mollin, D. L. *Brit. J. Hæmat.* 1957, **3**, 253.
9. Spray, G. H., Reynell, P. C., Taylor, K. B. Communication to the Medical Research Society, 1957.
10. Booth, C. C., Mollin, D. L. Unpublished observations.

## PNEUMOCONIOTIC NEUROSIS

SIR,—I had hoped that a better-informed champion of the pneumoconiosis panels might have rallied to their defence; in his absence, perhaps I may be allowed to refute some of the implications in Dr. Grunwald's letter of Oct. 26.

The experience on which I draw extends only to coalminers, and the "area" to which I referred (Oct. 12) is an entirely arbitrary one containing twelve pits, and has nothing to do with any other geographical area on which the Ministry of Pensions and National Insurance may base its figures. I feel Dr. Grunwald should therefore make more certain of his ground. In my original letter I said that it is the practice of our local panel to do a full clinical examination including an exercise-tolerance test. I can only reiterate that this is true. Dr. Grunwald, however, shifts the argument on to a much wider basis, and makes a statement which is open to grave doubt—i.e., "it is not correct that all insured persons claiming industrial-disease benefits for pneumoconiosis are examined by a member of a pneumoconiosis panel."

The facts in the Sheffield region are these.

Everyone making a claim for benefit on the ground of pneumoconiosis is radiographed locally, and relevant particulars are taken; the full-sized plate is then forwarded to a member of another pneumoconiosis panel operating in another area. He reads the plate and gives what is expected to be an unbiased opinion on it. It is then the responsibility of the Ministry of Pensions and National Insurance to inform the applicant of the opinion and at the same time to say that he is perfectly free to appeal against this to his local panel if he so wishes. If he is dissatisfied and appeals, he is fully examined ("1st examination") by the local panel, under the conditions I described.

It is becoming a common practice in this region for mining applicants to use this form of preliminary radiography in preference to attending at a mass-radiography unit. Each applicant knows that if the "preliminary radiograph" is rejected he has a right of appeal, and therefore goes periodically for a check-up with this in view. Most are satisfied with their periodical radiograph, but a number do take advantage of appellation.

In South Wales, where the interest in pneumoconiosis first centred, this system seems to have flowered into full maturity; hence South Wales figures in rejection of "preliminary radiographs" are much higher than the 20% of the Sheffield area, and no doubt contribute largely to swelling the national figure that Dr. Grunwald quotes.

It would appear, therefore, that not all rejectees are first applicants; they fail, therefore, to form such a hotbed of dissatisfaction as your correspondent would imply, but from them certainly can be distilled the small but vocal minority which has impressed Dr. Macdonald (Oct. 19).

I feel I am on safe ground in disagreeing with Dr. Grunwald's statement that the main reason for miners continuing to work down the pit is lack of suitable alternative employment. Miners continue to work down the pit with minor degrees of pneumoconiosis because they are perfectly well able to do so, and these jobs are still among the highest paid in industry. The miner as a rule has no desire to change his home surroundings or alter his routine to go to "alternative and suitable employment," though he is of course free to do so if he wishes. Dr. Grunwald further bases his argument on such questionable things as newspaper reports to try and prove that the pneumoconiosis panels under present conditions are at least as productive of neurotics as they are of satisfied customers;

in my experience the " pneomoconiotic neurotic," so far as the mining industry goes, is an exception.

Surely the kernel of the argument has nothing to do with the methods of examination of individual panels but is much more clearly stated in Dr. Macdonald's letters of Sept. 28 and Oct. 19—i.e., is both a practicable and fresh approach needed ?

In the first place your correspondents seem to ignore entirely the political origins of pneumoconiosis benefit and the machinery set up to deal with it. It is hardly surprising to me that the planners of the system were overimpressed by radiographs, but I have no doubt that pneumoconiosis panels as a whole do a good job in modifying this overemphasis in the light of the M.R.C. report which Dr. Grunwald quotes. It may be high time that some changes should be made ; a change in the definition of the disease as given in the Act would be helpful, and perhaps in the composition of panels from time to time—e.g., individuals might serve in varying parts of the country. But this is only picking at the problem, and Dr. Macdonald's proposed commission of inquiry would only confuse the issue further.

Wherever pneumoconiosis is, surely there must be a number of medical men who must assess its degree and its effect on function according to local conditions by means of a full clinical and radiographic examination. The fact that there is superimposed a body of Civil Servants who handle the paperwork may be reprehensible, but so far as I am aware the local panel is not subject to bureaucratic interference, and works in complete clinical freedom. I find it difficult to imagine them as a collection of medico-administrative myopes, gathered together in hot debate over some X-ray plate whilst hapless and unexamined rejectees fume in dyspnœic frustration in the far distance.

Having postulated a panel, let us by all means have a " new approach " for them to work under. In the smoky industrial cities of the north, examination of routine radiographs of non-mining adults will disclose an unusual amount of mild bronchitis and emphysema ; similarly, routine radiographs of non-complaining miners will disclose mild pneumoconiosis. It would not be stretching credulity too far to consider bronchitis and emphysema one of the hazards of existence in an industrial town, as pneumoconiosis is a hazard of mining ; but neither of these diseases gives rise to disability until it becomes severe, and here I am at variance with Dr. Macdonald. I do not agree that a high prevalence of bronchitis and emphysema among miners is so much attributable to their jobs in the pit as to the fact that they live in smoky surroundings outside it. The fact that they have been down the pit any length of time is disclosed by the fine reticulation and nodulation which forms the picture of mild pneumoconiosis ; if this is combined with the bronchitis and emphysema nurtured above ground, the two diseases give rise to disability at varying periods late in working life.

I would hasten to assure Dr. Macdonald that modern pit-ventilation does much to disperse dust ; at the same time it throws at the miner air which is drawn from the surface and may have had some of its gaseous impurities adsorbed on road-way walls on the way down. Hence, during part of his shift, the miner may be in a purer atmosphere than if he were in his local picture-house or pub. How then, with the best of intentions, is one to assess what proportion of the disability is due to working conditions and how much is due to living conditions ?

Let the " new approach " be an all-embracing one. Because the miner lives in dirty surroundings on the pit-top, making him bronchiectatic and emphysematous, and works underground making him pneumoconiotic, so let him by all means be compensated ; but then why not many others who live in industrial cities for the sake of doing jobs productive of chest diseases ? A bus conductor, for example, because it may be argued that he is more prone to tuberculosis than others. I doubt whether Dr. Macdonald's forward-looking ideas will make much headway until we are ready to take this more idealistic view.

It may well be that the purer atmosphere of South Africa will simplify matters, and that bronchitis and emphysema may not be as common either clinically or subclinically as they are in England. Their miners, I believe, are largely Negroes, who may not be so resistant to tuberculosis, which undoubtedly plays a large part in the complicated massive focal fibrosis that is all too common here. Perhaps their mines are tunnelled through more siliceous rock, or their ventilation systems are more advanced; at all events our South African panellist is bound to have his own particular problems, which are not going to be made any easier by launching him under the ægis of " pulmonary disability " rather than " pneumoconiosis."

Dr. Grunwald rightly yearns for an " objective test as a basis for assessment "; it has taken the M.R.C. Pneumoconiosis Research Unit at Cardiff nearly two years to produce a machine which is accurate, reasonably robust, and portable, with which to do this very test. The machine is now, I believe, approaching the end of its trials ; no doubt it will form a helpful part of the armamentarium of pneumoconiosis panels in the future. Will it, I wonder, prove as individually useful as a painstaking clinical examination, or an exercise-tolerance test, or a good radiograph ?

Barnsley, Yorks. J. D. M. HOLT.

## COMPARISON OF CARDIAC AND PYLORIC SPHINCTERS

SIR,—I read with much interest the paper by Dr. Atkinson and his colleagues last week. They were surprised that the pylorus is normally relaxed. May I draw attention to certain well-established observations ?

From theoretical considerations it may be deduced that the pylorus is patent at rest.[1] This has been confirmed by the balloon method [2–3] and by gastroscopy.[4–7]

That the pylorus does not control gastric evacuation has been shown in experimental animals,[8–10] and in the human [11] or by cannulation.[12]

At a meeting of the Physiological Society at Cambridge in 1954 I indicated that the function of the sphincters of the alimentary canal can be deduced as a corollary of the law which governs the behaviour of the peristaltic wave, and gave reasons why the sphincters act in two ways—namely, *passively* as anatomically undifferentiated structures in the forward transmission of the peristaltic wave, and *actively* as functionally specialised structures in the prevention of reflux of the intestinal contents at critical junctions.[13]

It should be noted that the antrum, the pylorus, and the duodenum act as a functional unity [14] and that their coordinated relationship is not altered by vagotomy.[2]

I dealt briefly with the cardiac sphincter in a communication at the meeting of the French Gastro-enterological Society in Paris [15] when the subject of œsophageal reflux was discussed ; and I studied in some detail the behaviour of the pyloric sphincter in my recent monograph.[16]

London, W.1. J.-JACQUES SPIRA.


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## A SUSPENDED BED FOR POSTURAL DRAINAGE

SIR,—I regret that in my article of Oct. 26 I omitted to say that the bed actually shown and used so far is the 'Lawson Tait' bed (using two foot-ends), as designed by S. B. Whitfield & Co. Ltd., for the Royal National Orthopædic Hospital at Stanmore.

Institute of Orthopædics,
Royal National Orthopædic
Hospital, Stanmore, Middlesex. A. B. KINNIER WILSON.

## TREATMENT OF BRONCHITIS IN PATIENTS WITH RESPIRATORY-MUSCLE PARALYSIS AFTER POLIOMYELITIS

SIR,—I was much interested in Dr. Kinnier Wilson and Dr. Harwood Stevenson's report (Oct. 26). Since reading their first article in 1952, we have been making use of the methods they described in that article, but have not used trypsin or isoprenaline by aerosol inhalation.

We have been struck by the fall in the vital capacity in these patients when they develop a chest infection, even when radiographs showed no evidence of collapse. This fall in vital capacity much reduces the power of coughing.

In addition to the methods described by Dr. Kinnier Wilson and Dr. Harwood Stevenson, we have been using a further one to increase this power in suitable cases. The patient's lungs are first inflated with a mask and the Oxford inflating bellows; chest compression by the physiotherapist is then able to produce powerful coughing. This has often been of great value, and in fact on one occasion was life-saving in a patient whose breathing was obstructed by a large amount of mucus.

Ham Green Hospital,
Pill, near Bristol. R. V. WALLEY.

## ACUTE RHEUMATIC FEVER IN CHILDREN

SIR,—I have read with great interest the careful comparative analysis of six forms of treatment of rheumatic fever by Professor Illingworth and his colleagues in your issue of Oct. 5.

Their summary statement that "cortisone cases fared better than all other cases with respect to carditis," and the additional observations that none of the children had arthritis for more than 5 days after starting treatment, and that rheumatic manifestations did not develop after the first week of therapy, confirm our observation that hormone therapy arrests progressive symptoms of rheumatic fever.[1]

We observed that in children with an onset of less than 2 weeks, carditis was arrested in 24–72 hours and terminated by the end of a week of therapy, and that children were ambulatory 2–3 weeks after therapy. However, the daily amount of hormone given for 7 days was about twice that given for the first week in the Sheffield report.[2]

I would agree with Professor Illingworth and his colleagues that sufficient evidence has accumulated to indicate that children with rheumatic carditis should receive adequate hormone therapy as soon as possible after the onset of carditis. Our own studies indicate that, for early cases, a week of therapy in adequate dosage is sufficient.

Department of Pediatrics,
New York Hospital—
Cornell Medical Center, New York, 21. MAY G. WILSON.

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# Parliament

### Legislative Programme

THE new session of Parliament was opened on Nov. 5, and in the Speech from the Throne it was announced that Bills would be introduced to improve the arrangements for the industrial reablement, training, and resettlement of the disabled, and to authorise increases in retirement and other benefits and in contributions under the National Insurance and Industrial Injuries schemes. War pensions are also to be increased, but this can be done under Royal Warrant and will not need fresh legislation. The laws relating to the adoption of children and the supervision of those who take children into their care for payment are to be amended. The Government propose to continue to study the "wider problems for the provision of old age" and penal reform and the treatment of offenders. They hope to improve the prison system in the light of an "imaginative programme of research."

### Pension Increases

THE Bill to implement the increases in pensions and benefits was introduced on Nov. 6 and received a second reading on Nov. 13. Under it the standard rates of National Insurance retirement pension at minimum pension age, and of unemployment and sickness benefit, are to be raised from 40*s.* for a single person to 50*s.* and from 65*s.* for a married couple to 80*s.* The new standard rate of widow's pension will also be 50*s.* The widowed mother's allowance including the payment for the first child, will go up to 70*s.* Under the Industrial Injuries Scheme, the standard rate of injury benefit and of the 100% disablement pension will be increased from 67*s.* 6*d.* to 85*s.* The widow's pension of 45*s.* will be raised to 56*s.*

When these new rates begin it is intended to repeal the tobacco-token scheme which has been much criticised. Instead non-contributory old-age pensioners will receive a special addition to their pensions of 2*s.* 4*d.* a week, the cash equivalent of the tobacco token. The increased benefits and pensions will have to be taken into account in calculating assistance grants to those who are drawing supplementary assistance. But the assistance scales are to be increased from Jan. 27. The proposed increases, which take into account the repeal of the tobacco token scheme, are 5*s.* a week for a single householder and 9*s.* for a married couple, with appropriate increases to the other rates.

The higher rates of pensions and benefits under the National Insurance Scheme, together with the increase in Industrial Injuries benefits will add about £177 million in the first full year to the expenditure of the two Funds. Accordingly, the contribution paid by the employed man will be increased by 2*s.* to become 9*s.* 5*d.* and that paid by his employer by 1*s.* 11*d.* to become 8*s.* 1*d.*, including in each case the separate National Health Service contribution. The contribution for the self-employed man will be increased by 2*s.* 3*d.* to become on the same basis 11*s.* 6*d.* The increases in contribution will carry with them an immediate increase of about £35 million a year in the supplement from the Exchequer. The Bill will also increase substantially the long-term Exchequer liability.

The Royal Warrant is being amended to raise the basic rate of war pension for 100% disablement by 17*s.* 6*d.* a week with proportionate increases for the less severely disabled. There will also be increases in the rates for widows and in some supplementary allowances. The additional cost to the Exchequer will be £16½ million in a full year.

### The Minister and Whitley

ON Nov. 6 in the debate on the Queen's Speech, Mr. L. J. CALLAGHAN asked how the Government intended to relate wages to productivity in the public services. How for instance was the probation officer's productivity to be measured? Had he to reform more criminals? What about nurses? Were they to nurse more patients, or was the test to be more beds per nurse? Where the Government were interested in wage claims, were these claims to be considered on their merits or were the Government saying that, whatever their merits, the economic position of the country was such that they could not be conceded? It seemed that the second test had been applied to health-service employees. Everyone knew that the public services were never in the vanguard of wage increases. They were always at the end

of the queue. The health-service employees were not only behind industry in their claim, they were behind the Civil Service and the local authorities. If anybody had established a claim on equal comparisons it was this particular group of people; yet this was the claim which the Government had chosen to make a test case.

In the course of the debate Mr. DEREK WALKER-SMITH, the Minister of Health, agreed that a claim had to be looked at on its merits—but on its merits not in an isolated context, but in the general context of the economic situation, including the necessity to counter inflation. The staff in question had had their last pay increase of 3% with effect from Jan. 1 last, or in some cases from the preceding month. Since then the cost-of-living index had risen somewhat. There was no dispute about those facts. The question really was whether such a short-term adjustment was compatible with the policy of halting inflation. On that, it seems that common sense and experience combined in saying "No." He added that to describe the Whitley Council's recommendation as unanimous was misleading. The management side of the council was composed of 10 representatives of hospital authorities, 3 representatives of executive councils and 5 departmental representatives. The 5 official departmental representatives had never approved this increase. They had opposed the offer on the grounds of the general economic context, and they voted against it. Further, the unofficial majority on the management side, if he might so describe it, were left in no doubt that approval might well have to be withheld from this agreement.

Mr. R. J. MELLISH asked if it was not a fact that the main basis on which this claim had been conceded was the terrible problem of the shortage of staff. How were we to overcome the shortage of staff if this claim was not met? Mr. WALKER-SMITH agreed that this was an important consideration. It was one of the considerations which had to be taken into account, together with the general economic considerations. It was a very difficult question and it had caused him great personal anxiety and difficulty to decide what was the right course.

Dr. EDITH SUMMERSKILL reminded the Minister that the health-service workers were not producers. Neither could their claims be related to saving. Nurses were some of the lowest-paid workers in the whole country. When a Whitley Council recommended an increase for nurses, could the Minister assure the House that the action taken with respect to this Whitley Council recommendation would not be repeated? Mr. WALKER-SMITH agreed that the question of people who were not directly productive was important. The general test of productivity with which he was concerned for this purpose was the overall test that money incomes should not increase faster than productivity. But in an expanding economy there should, of course, be scope for improving prospects for those who did socially useful but not directly productive work. He was satisfied that this decision had to be taken in relation to the general economic context and could not reasonably or sensibly have been taken in isolation from it. These were the sort of workers who would suffer in an unrestrained inflation, not perhaps most of all—because those who would suffer most were the pensioners, the retired people, and the fixed-income people—but they formed a sort of middle category, and obviously would suffer more in an inflationary race than the mass of industrial workers, with their massive position in the economy and their greater bargaining power. In his view there was no direct antithesis here between the interest of these people and the general interest, because it was in their interest, as well as in that of the community as a whole, that inflation should be held. It was with this consideration in mind that he had had to withhold approval from this agreement, but with an undertaking to review it at an appropriate time.

In an answer to questions Mr. Walker-Smith said that the cost of implementing the agreement would have been about £604,000 in a full year. He intended to publish Sir Noel Hall's report on the administrative structure of the hospital service in about a fortnight. The report was at present before the Whitley Council, and there was no reason for anyone to infer that no action would be taken on the report.

# Medicine and the Law

## Postoperative Tetanus

A man of 53 died from tetanus after a minor operation at Boscombe Hospital on Sept. 25. At the inquest the hospital pathologist said it was almost certain that the organism entered the wound during the operation. A subcommittee of the Bournemouth and East Dorset hospital management committee, after inquiring into the death, have now announced that they found "no evidence to show how there was a breakdown in the usual aseptic precautions," nor how the organisms entered the wound.[1] Among the subcommittee's recommendations was one that every effort should be made at all times to prevent contaminated air from getting into the operating-theatre.

# Obituary

## RICHARD WARREN

D.M., M.Ch. Oxon, F.R.C.S.

Mr. Richard Warren, who died on Oct. 31 at Weston-super-Mare at the age of 81, had practised surgery in London and in the West Country.

The son of General Sir Charles Warren, G.C.M.G., he was educated at Charterhouse, New College, Oxford, and the London Hospital. At all three he held scholarships, and he took first-class honours in natural science in his B.A. degree in 1897. After qualifying in 1900, he was awarded a Radcliffe travelling fellowship, and in the next year he continued his medical studies at Berne and Vienna. After he returned to this country he took his D.M. in 1905 and his M.CH. in 1907. In 1906 he became surgical registrar at the London Hospital with Frank Kidd, and he held this post till he was appointed to the staff in 1909. In those days the registrars were not allowed to operate; and when Warren came on the staff the absurdity of this was shown when, in the first fortnight, he performed a hundred major operations with outstanding success. A large and powerful man, he was a heavyweight boxer, and the skill and delicacy of his operating was the more remarkable.

In the 1914-18 war he served in the British Expeditionary Force with the R.A.M.C. Soon after he returned to civilian life he decided to give up his appointments at the London Hospital, the Brompton Hospital, and the Shadwell Children's Hospital, and in 1921 he moved to Weston-super-Mare. Of his years there K. C. M. writes:

I first met Warren twenty-five years ago when, as a brash, over-confident, and ignorant young house-surgeon, I arrived at Weston-super-Mare. He treated me with a kindness and courtesy I did not deserve and was ready to listen and discuss a case as an equal. We were always being astounded by the wealth of his knowledge, and often when some new procedure was written about he would remark with a twinkle in his eye that So-and-So had written about that in 1912, quoting date and journal. He was for ever learning and was always enthusiastic about new methods and techniques. He was a brilliant diagnostician and operator, and his handling of the inflamed intestine was a joy to watch. He was one of the last great general surgeons and was well equipped to tackle any surgical problem in all parts of the body. His wit was ever present, but never at the expense of others, and in all the years I knew him I never heard him say an unkind word about anyone. He enlivened his conversation with countless anecdotes of great men, for his experience covered the years from the days of frock-coat operating to the advent of antibiotics. He was a born teacher, and, although not a good speaker to a large audience, he was able to pass on his knowledge and experience to anyone interested in learning.

His interests were many and ranged from music to boxing, fishing, and shooting. One game he never mastered was golf, and he used to say he was the second worst doctor golfer, the late medical officer of health for Weston-super-Mare being in his opinion the worst. He was an excellent shot and a good fisherman; both pastimes were his hobbies, but I think his

1. *Manchester Guardian*, Nov. 8.

love of music was second only to his love of surgery. On his retirement he began to learn and study the songs of Schubert, and he lately told me that he knew over a hundred and fifty songs by the great master. His musical god was Beethoven, and he was prepared to defend that contention against all comers. He was a humble man, as only a great man could be, and it was an honour to have known him, worked with him, and been counted as one of his friends. He was indeed the complete man.

N. C.C., another of his colleagues at Weston, also recalls his disarming humility.

Dicky (he writes) was always willing to help with his sound opinion, which was given almost apologetically. One felt that one could go to him for help and advice, receiving understanding and valuable assistance, given with the wisdom born of sound knowledge and experience.

He had a deep sense of humour and his anecdotes and reminiscences, which were many, were told in a quiet voice which gave them added charm. In his leisure he got recreation from shooting and fishing, and even in his seventies he was often to be seen on the mudflats at dawn or dusk, looking for duck and snipe. He was also a musician and his knowledge and appreciation of classical music were of a high standard. In fact, he was so widely informed that there was scarcely a subject he could not discuss without obvious understanding and some authority.

Mr. Warren married in 1912 Violet Irene Jenkin of Heamoor, Cornwall. She died in 1941 and they leave two sons and a daughter.

## GEORGE HERBERT COLT
M.A., M.B. Cantab, F.R.C.S.

Mr. Colt, who died at his home near Guildford on Oct. 26 at the age of 79, began his surgical career while still a student at St. Bartholomew's Hospital, when he designed his apparatus for the treatment of aneurysm.

He was born at Hampstead, the son of Frederick Hoare Colt, and he was educated at Tonbridge School and at Sidney Sussex College, Cambridge, where he took a first-class in the natural sciences tripos in 1900. After qualifying from Barts in 1904 he held house-appointments there and at the Derby Royal Infirmary. In 1908 he took the F.R.C.S., and in 1910 he was appointed assistant surgeon to the Royal Infirmary, Aberdeen, and assistant to the professor of surgery there. At the beginning of the 1914-18 war, with his chief, Sir John Marnoch, he was one of a group of doctors who formed themselves into the 1st Scottish General Hospital, and later he was one of the team who went to Salonika to become the nucleus of the 43rd General Hospital.

After the war Colt returned to Aberdeen, and in 1923 he was appointed full surgeon to the Royal Infirmary and lecturer in clinical surgery in the University. But he was not chosen to succeed Marnoch in the chair, and soon afterwards he returned to London and set up in practice in Harley Street. Later he joined the staff of the Gravesend and North Kent Hospital. Though he continued to work in the South until he retired, he returned every August to Deeside to fish.

Of Colt's contribution to surgery S.M.C. writes:

His inventive mind showed itself in the manner in which his final apparatus was produced. He first of all devised a machine to deliver, through a cannula, long lengths of "snagged" (milled or roughened) wire. He then proceeded to devise a cutting guillotine device which could divide the wire whilst the cannula was still in the aneurysm. In both procedures there was the hazard of the wire travelling into the main aorta stream. Finally he produced the ingenious wire cage which folded into an umbrella, and which, when floating in the aneurysm, circulated round and round like a sputnik. Its gossamer, delicate construction was perhaps its weakness. Unless clear of the laminated clot the umbrella failed to expand, and in one patient from St. Bartholomew's Hospital, who dropped dead outside the hospital a year after the operation, the well-opened umbrella was found without clot adherence. There were many lost battles, and, except for an astonishing case of Courcy de Wheeler, life was rarely prolonged more than a few years; but all who used it assure me that the relief of pain was spectacular.

In his work Colt had terrier-like tenacity of purpose, and for twenty years and more he spent every moment of his spare time in the study of necropsies on aneurysm and he collected some 707 cases. He never saw a case where natural cure had followed, and showed that at least 75% of patients with abdominal aneurysms were dead within two years. This, of course, does show that grafting surgery, despite its hazards, invariably needs strong consideration. But even if he had not designed his apparatus, his condemnation of the "morbid" management of aneurysms was in itself an achievement. He condemned and poured scorn on the régime of ten weeks of "8 oz. liquid and 10 oz. solids, with a pebble to suck when thirsty and a cheerful room of Southern aspect."

His other inventions are perhaps not as well known as they should be. Colt's needle—large, thin, curved, and extremely pliant—is a more or less standard instrument in many hospitals for the tension stitch or for the skin of the fat abdominal wall. He devised a distraction apparatus for fixing and holding the fractured ends ready for plating. The modern type of bone-drill owes something to him; for he was the first, as far as I can gather, to attach an interchangeable "pistol grip".

To operate on the tossing, heaving aortic aneurysm, with wall frail as a mulberry, and ready to burst from a trickle into a torrent, even today (with ample blood available) requires cool courage. What manner of man, then, was Colt? Small, bespectacled, with a round, unwrinkled face and a manner as gentle as the gossamer cage he planned for his operation, he showed that courage is not the privilege of any particular type. He might well have been an antiquarian (before television days), a librarian, or a research worker. To me he always seemed like the clerk Charles Lamb come to life; with his kindly mien, his gentle manner, and a whimsical piquant smile never far from the angles of his mouth. In surgical history the memory of this little man with great courage will remain as a milestone.

## ROBERT MAXWELL CHANCE
M.D. Aberd.

Dr. Chance, who died on Aug. 27, had been in practice in the West End for some forty years. He was chairman of the Euston branch of the National Service medical boards.

He was born at Battle, Sussex, in 1887 and was educated at Hymers College, Hull, and Aberdeen University where he excelled in boxing and rugby football. He graduated M.B. in 1910 and took his M.D. two years later. During the 1914–18 war he was a captain in the R.A.M.C. He was invalided out after suffering the effects of the first gas attack in 1915. For a short time he was resident medical officer at King Edward VII Hospital for Officers and then was in charge of the Freemasons' War Hospital. He started in general practice in London in 1917.

W. E. T. writes:

Many visitors from all over the world were fortunate enough to come under Max's care. He embodied all that was fine in medicine with his wise counsel, kindliness, and meticulous attention to detail. It was a well known fact that all patients referred by him to London hospitals were correctly diagnosed no matter how complicated the medical problem. He appeared to be always right.

Mrs. Chance survives him with their daughter.

# Appointments

BEVERIDGE, ELSPETH V., L.R.C.P.E., D.P.H., D.OBST.: assistant M.O., Inverness-shire.
CHURCH, I. C., M.R.C.S., D.P.M.: assistant psychiatrist (S.H.M.O.), De la Pole Hospital, Willerby, near Hull.
FOX, D. L., M.B. Manc., D.P.M.: county psychiatrist, Staffordshire.
JACKSON, DANIEL, M.B. Glasg., D.P.M.: consultant psychiatrist, child guidance service, school health service, Manchester.
MORRISON, A. B., F.R.C.S.E.: consultant orthopædic surgeon, Nottingham General Hospital.
MUKHERJEA, T. K., M.B.: senior casualty officer, Royal Infirmary, Halifax.
STREET, D. R. K., M.B. Leeds, D.P.M.: deputy medical superintendent (consultant), Rampton Hospital, Retford.
WILSON, A. S. M., L.R.C.P.E.: school M.O., Co. Durham.

# Births, Marriages, and Deaths

## BIRTHS

MURPHY.—On Nov. 4, to Dr. Isabelle Murphy and Dr. Grahame Murphy—a son, Jocelyn William, a brother for Gretta, Christopher, and Bridget.

## MARRIAGES

RUEBNER–MAUTNER.—On Oct. 26, in Halifax, Canada, Boris Ruebner, M.D., to Miss Susan Mautner.

# Notes and News

## ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS

THE foundation stone of the new College building at Sussex Place, Regent's Park,[1] was laid by Queen Elizabeth the Queen Mother on Nov. 6. The Queen Mother spoke of three men who had brought great distinction to the College: the late Sir Charles Read, president at the time of his death on Aug. 21; the late Sir William Gilliatt, also a former president; and Sir Henry Simson "whom I and thousands of his patients remember with affectionate gratitude." The president of the College, Prof. A. M. Claye, recalled that on Dec. 5, 1932, the Queen Mother, then Duchess of York, had opened the College house in Queen Anne Street. She was now showing her continued interest by laying the foundation stone of its new home, to be named Nuffield College after "our most munificent donor." Mr. Arthur Bell, honorary treasurer of the College, invited the Queen Mother to accept, as a memento of the occasion, a gold powder compact bearing the College arms. Mr. Ian Jackson, the honorary secretary, read a list of the contents of the casket which had been placed under the foundation stone.

At the annual dinner later in the day, The College was proposed by Lord Salisbury. Since the foundation of the College in 1929 the maternal-mortality rate had fallen from about 4·5 per 1000 total live and still births to 0·6 in 1955; and Lord Salisbury was sure that the standards set by the College had played a considerable part in that improvement. By its rugged effort to stand on its own feet and to remain free of Government control, the College had shown that it wanted to be in a position to speak freely about the National Health Service. It was principally a research body, and research, Lord Salisbury observed, was not a subject suitable for direct control by Government departments, which were inclined to take the short-term view; the danger that research would be starved by departmental control had been avoided by putting a non-departmental Minister, the Lord President of the Council, in charge of the Medical Research Council and other research bodies. Lord Salisbury hoped the College would be firm in its resolve to remain free of Government control. Referring to the new building and the work to be done there, he said that Industry should put its hand in its pocket to ensure that this great new enterprise got the support it deserved.

More money is needed to furnish and endow the new building, and, in his reply, Professor Claye declared that faith and hard work would be needed to ensure that the Nuffield College became "a creed in stone," a visible sign of the principles for which the Royal College stood. He spoke of the great contributions made to the new College by Sir Charles Read, and of the tremendous efforts of Lord Weeks, president of the appeal, and many fellows and members who devoted much time to College affairs. Prof. Bruce Mayes, chairman of the Australian regional council of the College, brought greetings and good wishes from fellows and members in Australia, and he read encouraging messages from the other regional chairmen—Mr. Arthur Nash (Canada), Mr. T. R. Plunkett (New Zealand), and Prof. James Black (South Africa). A very large company of guests at the dinner were cordially and entertainingly greeted by Prof. W. C. W. Nixon; and Mr. Richard Thompson, parliamentary secretary to the Ministry of Health, responded on their behalf.

## THE MINISTER AND WHITLEY

ON Nov. 11 a deputation of representatives from the management and staff sides of the National Health Service Administrative and Clerical Whitley Council saw the Minister of Health. Both sides assured the Minister that the pay increase for hospital officers which the council had recommended was not a part of a new inflationary wage cycle but only an interim settlement pending a general revision of the pay structure of the whole hospital administrative service.[2] The management side asked the Minister to change his mind in the interests of recruiting and efficiency, and the staff side deplored his admission that he had instructed his official representatives to oppose the claim before it had even been discussed in the council (see p. 1009).

The Minister replied that he could not change his decision, which had been made with regret. In the wider context of the country's economy and the Government's intention to check inflation he had no alternative but to defer approval of the council's recommendation. He repeated his promise to review the matter later.

After the meeting with the Minister the emergency committee of the National and Local Government Officers' Association (NALGO) instructed the 30,000 administrative and clerical N.H.S. workers who are their members to stop all overtime work from Nov. 18 as a protest against the Minister's refusal to withdraw his veto on the agreement.

1. See *Lancet*, Nov. 9, 1957, p. 945.
2. *The Times*, Nov. 1957.

## CALOUSTE GULBENKIAN FOUNDATION

THE Foundation's second list of grants, published on Nov. 8, contains no grants to science and medicine in the United Kingdom; but £36,000 is to be given, over the next three years, to the Sanatorium of Azounieh in Lebanon to build, equip, and run a research centre for chest diseases; and the medical faculty of Lisbon University is to receive £41,000 for its laboratories of electron microscopy and of physiological chemistry. The Foundation's grants to charity include some which will be of interest to medical readers. The Telephone Samaritans of St. Stephen's, Walbrook, London, whose efforts to reduce the suicide-rate have been described in our columns,[1] will receive £3000 a year for three years for the expansion of their work. £2000 has been offered for a two-year experiment of appointing a trained social worker to study the mental and material needs of people living in a common lodging-house.

## THE NATURE OF MAN

IN a sermon at the annual service of the Society of Apothecaries of London last month the Rev. M. F. FOXELL, their chaplain, spoke of three aspects of the study of man—the physical, the social, and the spiritual. The first considers him as a part of the animal creation, with a larger and superior brain which he has used to think in ways unknown to other beasts. The second sees him as a social creature that has developed ways and means of constructing what we call civilisation—a gregarious creature attempting to devise an acceptable way of life for the whole human race on one universal system. In Communism it is the system that matters most, and, until perfection is reached, each generation must suffer (so it is argued) for those that come after. On the third view man is a unique being, possessing some characteristic that transcends both his animal nature and his capacity to live rationally in the society of his fellow creatures. He is an immortal soul, capable of communion with God who has made him and all the world, and potentially able to inherit eternal life.

Psychology shows how these three aspects are in fact inseparable: the nature of man requires the coordination of body, soul, and spirit in harmony. The physical side of living is always with us: we have to breathe, eat, and drink, and, as far as possible, to keep fit. But fit for what? Fit to take a proper place in an ordered society for the general welfare of that society. True, but the word "welfare" does not cover everything in society. "Let us train more children to be scientists" is the call to the schools today. That is no doubt necessary for the fulfilment of the second aspect of man—to make him useful in all the needs of modern civilisation in peace and, alas, in war. We want people able to pursue the sciences further and to use and develop new devices so that they can do the work which our ways of life demand of us. But, now that the whole trend of society urges mankind to extravagances of invention that seem to outpace him, we are beginning to ask "Can man stand up to his own creations?"

There is, beyond this, an ultimate truth about mankind in which neither science nor Communism is interested—namely, that every man, woman, and child is a person. It is easy and convenient to put people into groups and to treat them so—the 11+, the teenagers, the employees, the employers, and, all together, the State or mankind as a whole. But doctors have learnt to beware of generalisations and attend to the particular; and by the Christian standard this applies to every human relationship.

The all-important truth about mankind is not to be found in science or in the economics of society but in the assurance that everyone, whatever colour his skin, has a spiritual nature, an immortal soul, as surely as he has his animal nature. "We are social creatures," concluded the Chaplain, "but our ultimate society is a heavenly one."

1. Varah, C. *Lancet*, 1957, i, 584.

In one at least of his congregation this sermon recalled the famous words of Winston Churchill in his Romanes lectures of 1935: "There are secrets too mysterious for man in his present state to know—secrets which once penetrated may be fatal to human happiness. But the busy hands of the scientist are already fumbling with the keys of chambers hitherto forbidden to mankind. Without an equal growth of mercy, pity, peace and love, science itself may destroy all that makes human life majestic and tolerable."

## CONTRACEPTION

The first lecture to be given under the Oliver Bird Trust [1] was delivered at University College Hospital Medical School on Nov. 6 by Dr. T. Mann, speaking on the biochemical basis of spermicidal activity. It was sponsored by the Society for the Study of Fertility, and Dr. A. S. Parkes presided.

Dr. Mann classified a wide range of compounds according to their mode of action upon spermatozoa, and drew attention to ways in which reversible inhibition of motility in vitro might be mistaken for spermicidal activity in vivo. He emphasised the importance of recognising that chemical contraception is not identical with spermicidal activity, and how little is yet known about the biochemical problems of clinical contraception.

Before the lecture the Council for the Investigation of Fertility Control, set up by the Oliver Bird Trustees in conjunction with the Family Planning Association, held its first meeting, to discuss the purpose and scope of the Council and the organisation of tests and clinical trials of contraceptives.

## MENTAL WELFARE IN SCOTLAND

FIVE years ago the Scottish Advisory Council on the Welfare of Handicapped Persons set up a committee to inquire into the welfare needs of the mentally handicapped. The committee's report has now been printed.[2] Dealing with the mentally ill and the mentally defective, it takes note of the strain which the care of them throws on their relatives. The committee realises that not all its suggestions can be acted on at once, but it recommends for immediate action the ascertainment of those in need of care, the development of cooperative arrangements to ensure that those in need get all available services, and the encouragement of voluntary services.

Many defective patients are capable of employment (either at home, in special workshops, or in the wider world), and registration as disabled persons would often be helpful. Suitable jobs in hospitals, the reports suggests, would enable them to work under supervision. For the young, more special schools were needed, including residential schools for those with unsatisfactory homes. For older defectives, hostels would serve as halfway houses between institutions and life outside, and as a means of giving respite to their relatives; as many as possible should be boarded out where conditions were suitable. Local authorities should be urged to arrange after-care schemes.

Mental illness may be a potential rather than an actual handicap at a given moment; there were patients not well enough to lead a normal life nor ill enough to have to stay in hospital, and training establishments and resettlement units with visiting psychiatrists were useful in educating them. There was a great need, the report adds, for after-care homes outside mental hospitals. Clubs for old people might help to prevent mental illness.

The committee holds that the public, especially parents, are not fully aware of the services available, and the actual or possible services should be suitably publicised.

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### University of Oxford

On Nov. 2 the degree of D.M. was conferred on G. E. Honey and A. L. Jacobs.

### University of Cambridge

On Nov. 2 the following degrees were conferred:

*M.D.*—J. E. Blundell, I. J. Carré, E. W. P. Jones.
*M.B.*—*J. V. F. Catto, R. O. S. Sims.
*M.A.*—J. G. Cruickshank.

* By proxy.

1. See *Lancet*, Sept. 28, 1957, p. 652.
2. Department of Health for Scotland. The Welfare Needs of Mentally Handicapped Persons. H.M. Stationery Office, 1957. Pp. 25. 1*s.* 3*d.*

### Royal College of Obstetricians and Gynæcologists

The following have been admitted to the membership:

George Adams, Norman Allan, J. P. Alvey, R. D. Atyeo, Salar Akhtar Aziz, J. D. Baeyertz, Victor Benatar, G. K. Bernays, W. P. Black, Wei Chew, H. D. Chomse, Agnes Clark, R. B. Conyngham, Leela Mahadeorao Dhadphale, I. P. Dunnett, P. F. M. Du Toit, A. A. Earn, Luba Epsztejn, Frances M. Fountain, David Friedberg, Dorothy M. Gratton, D. E. Gunatilleke, A. D. Hewson, B. K. Higgins, Vera Hingorani, A. N. Horwitz, Mary H. Hutcheon, E. G. Jonas, I. H. Kidd, D. J. Lancaster, Mary E. Larg, Martin Lesser, T. S. Macdonald, C. N. McFarlane, Lajja Mehta, H. A. Milne, B. J. Murphy, P. R. Norris, T. C. O'Connor, C. E. Parr, A. B. L. Peake, R. P. C. Perrott, Patricia M. Russell, Anne P. Ryan, G. T. Smedley, J. H. Spurway, D. A. Thatcher, G. H. M. Wallace, J. H. Walters, M. B. Wingate, E. C. Wood.

### Royal College of Physicians of Edinburgh

At a meeting of the college held on Nov. 5, with Sir Stanley Davidson, the president, in the chair, the following were elected to the fellowship:

J. A. Hislop, William Goldie, R. F. Thomas, Rabindra Nath Chaudhuri, H. E. Taylor, R. J. Twort, J. W. Ferguson, J. L. Markson, H. V. L. Finlay, T. McL. Galloway, A. R. Currie, Cecil Harris, J. B. Lowe, J. F. Galpine, F. L. Ritchie, I. C. Gilliland, P. W. Hannay, J. W. Farquhar, N. R. Grist, A. S. Douglas, M. F. Oliver, J. D. Robertson, Mohammad Ayub Khan, D. G. C. Whyte, J. H. Bowie, A. G. Macgregor, E. B. French, J. A. Strong, G. J. Summers, J. McQ. Johnston, F. J. Wright, G. L. Montgomery, Alexander Kennedy, J. H. F. Brotherston, Kenneth Cowan, John Marshall, J. A. W. McCluskie, E. G. Oastler, Ian Gordon.

The following were elected to the membership:

S. Layinka Ayodeji Manuwa, J. H. Hutchinson, L. G. Topham, R. G. Paley, R. G. MacFarlane, Nirmal Kumar Sen, E. B. Naug, Sankar Prosad Das Gupta, Davendra Nath Gupta, Gnanamanickam Carl Anbu-Nathan, A. D. Macdonald, H. A. K. Rowland, Dwijendra Nath Bose, J. F. Boyd, W. D. Elliott, R. H. Scott, Jagdish Narain Singh, H. A. Aponso, L. K. Manning, Ratansinh Mehta, Myint Myint Khin, I. G. Johnston, C. G. B. Downie, A. de S. Lawrence, Geoffrey Howitt, Mohamed Salah Eldine Ibrahim, Isidore Reef, J. D. Frankish, B. J. Lemass, Satya Gupta, Syed Moinual Haque, T. H. Beare, P. J. Lipsitz, Nedjdet Gurgen Sanerkin, Hock Boon Wong, E. A. Cameron, W. J. H. Leckie, E. M. Ashenhurst, Max Traub, R. E. Cronje, J. P. Eckert, M. R. P. Hall, M. J. A. McDonald, D. H. Garrett, E. L. Fischer, G. L. Money, Govinda Krishna Warrier, John Ferguson, Samir Kumar Gupta, J. G. Sloman, R. W. B. Penman, Vincent Marks, A. E. Hugh.

### Royal Faculty of Physicians and Surgeons of Glasgow

At the annual meeting of the Faculty on Nov. 4, the following office-bearers were elected:

President, Prof. Stanley Alstead; visitor, Mr. Arthur Jacobs; hon. secretary, Dr. Gavin B. Shaw; hon. treasurer, Dr. J. A. W. McCluskie; hon. librarian, Dr. A. L. Goodall; representative on the General Medical Council, Dr. Andrew Allison; councillors, Dr. G. J. Aitken, Dr. W. Malcolm Gibson, Dr. D. McKay Hart, Dr. A. Cameron Macdonald, Dr. H. R. MacLennan, Mr. D. C. Miln, Mr. R. B. Wright, Prof. G. M. Wyburn.

### Royal College of Physicians of Ireland

At a meeting of the college on Nov. 1 with Dr. F. J. O'Donnell, the president, in the chair, the following were admitted to the membership:

M. W. Browne, M. W. P. Carney, P. J. Meehan, I. C. Roddie.

### Royal Commission on Mental Laws

The Government are now receiving comments on the report of this Royal Commission from local-authority associations, hospital authorities, and other interested organisations, and, though there is no provision for legislation in this session of Parliament, Mr. Richard Thompson, parliamentary secretary to the Ministry of Health, assured the National Association for Mental Health conference in Manchester on Nov. 8 that the recommendations are not being pigeon-holed. The Government had accepted the need for a revision of the law on broad lines, but many questions of principle and detail had still to be worked out. The suggestion to admit patients to mental-deficiency hospitals on an informal basis without using the present detaining procedure was now being considered.

Since the start of the health service progress had been made in the organisation of training for mental defectives at occupation centres. At present, Mr. Thompson said, despite financial stringency the service had high priority for limited resources. In 1948, 100 centres existed; today over 300. In 1951 just over 4000 boys and girls under 16 were receiving training; to-day well over 9000. Because most resources had been applied to mentally handicapped children, the more complex problems of adult defectives had not yet been properly studied. If training and social facilities could be provided for adults the experience so gained might considerably affect the training of children. With full employment and economic stringency it was difficult to provide staff and buildings, but this need not prevent a start being made.

### World Health Organisation

Dr. M. G. Candau, director-general of W.H.O., has accepted the tenth World Health Assembly's offer to renew his contract, which expires next July. He has asked for the renewal to extend for two years.

### Royal Society

The Copley medal has been awarded to Sir Howard Florey for his contributions to experimental pathology and medicine, and the Buchanan medal to Sir Neil Hamilton Fairley for his contributions to the control of malaria.

### French Ban on Import of Animals

The *Journal Officiel* (as reported in *The Times*, Nov. 8) has published a decree, to come into force next month, forbidding the entry into France of any living carnivorous animal from many countries, because of the increase of rabies. Britain is among the countries not affected by the decree.

### National Insurance Benefits for Hospital Inpatients

Changes, recommended by the National Insurance Advisory Committee, affecting the national insurance benefits or pensions of some husbands and wives receiving free inpatient treatment in hospital, come into force on Nov. 18.

Under existing rules, the allowance paid to a husband for his dependent wife—normally 25*s.* a week at present—as an addition to his own sickness or unemployment benefit or retirement pension, in most cases stops completely after she has been in hospital for about one and a half to two and a half years. Under the new regulations the allowance will be reduced by 7*s.* 6*d.* a week if the wife is maintained free in hospital for more than eight weeks. If she remains in hospital for more than two years, the allowance for her will continue to be paid, but at the reduced rate of 7*s.* 6*d.* a week (or 12*s.* 6*d.* if she is a tuberculous patient). The reason for the reductions is that the dependant's allowance is intended as a contribution to ordinary needs at home, and while a patient is receiving free maintenance in hospital, some of these needs—food for example—are being met by the National Health Service. Details are given in leaflet N.I.9 available in all local Pensions and National Insurance offices.

### Ministry of Health

Mr. Richard Thompson, parliamentary secretary to the Ministry of Health, has appointed Mr. G. C. Hulme to be his private secretary in succession to Mr. J. P. Cashman.

### Medical Bequests

The late Dr. Cuthbert Lockyer has left £5000 to the Royal College of Obstetricians and Gynæcologists to establish a fund for research or a travelling fellowship, and £5000 to the Royal College of Physicians of London to establish a scholarship or lectureship (or both) in diseases of childhood.

### British Institute of Radiology

This institute will hold its annual congress at the Royal Horticultural Halls, Westminster, from Nov. 27 to 29. Lord Cohen of Birkenhead will give the opening address on the physician's debt to radiology, and Dr. F. G. Spear will give the Mackenzie Davidson lecture on effects produced by radiation. The programme will include symposia on pulmonary hypertension, arc therapy with 250 kV X rays, and the effects of radium and radiostrontium deposition in bone.

### Children Going Into Hospital

A conference on the preparation and needs of children going into hospital will be held at B.M.A. House, Tavistock Square, London, W.C.1, on Thursday, Jan. 23, 1958. Prof. R. S. Illingworth will give the opening address and the speakers will include Dr. John Burton, Dr. Charlotte Naish, and Dr. G. F. Vaughan.

Further particulars can be had from the medical director of the Central Council for Health Education, Tavistock House North, W.C.1.

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Dr. G. F. Anderson has been appointed medical adviser to the Distillers Company (Biochemicals) Ltd. at Wimbledon.

## Diary of the Week

NOV. 17–23

### Monday, 18th

HUNTERIAN SOCIETY
8.30 P.M. (Apothecaries' Hall, Black Friars Lane, E.C.4.) Sir Francis Walshe, Mr. Douglas Woodruff (for), Lord Attlee, Dr. Bruce Cardew (against): A Full-Time State-Controlled Medical Service is Contrary to the Best Interests of the Patient.

### Tuesday, 19th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
3.45 P.M. Prof. R. J. Last: The Pectoral Girdle (Arnott demonstration).
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. J. A. B. Gray: Peripheral Mechanisms Underlying Sensations.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. Dr. R. A. Brews: Ætiology of Carcinoma Corporis Uteri.
ROYAL ARMY MEDICAL COLLEGE, Millbank, S.W.1
5 P.M. Mr. Harold Edwards: Crohn's Disease and Allied Disorders.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Queen's College, Dundee.) Dr. F. L. Mitchell: Urinary Steroid Hormone Assays and Their Clinical Value.

### Wednesday, 20th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.15 P.M. *General Practice.* Dr. Ronald Gibson: Management of the Hopeless Case.
POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
2 P.M. Dr. John Hardwicke: Proteinuria.
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Mr. C. W. F. Burnett: Disordered Third Stage.
INSTITUTE OF ORTHOPÆDICS, 234, Great Portland Street, W.1
8 P.M. Dr. R. J. Hasterlik (Chicago): Skeletal Changes in Chronic Radium Poisoning in Man.
INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5.30 P.M. Mr. Harvey Jackson: Intracranial Neoplasms.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. J. A. Dudgeon: Virus Diseases.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Mr. Donald Barlow: Problems Associated with the Construction of Heart-Lung Machines.
HARVEIAN SOCIETY OF LONDON, 11, Chandos Street, W.1
8.15 P.M. Mr. W. R. Winterton, Miss Joan Joshua, Dr. G. I. M. Swyer, Dr. Trevor Gibbens: Castration as a Therapeutic Measure.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. Mary Sheridan: The Young Deaf Child.
EUGENICS SOCIETY
5.30 P.M. (Royal Society, Burlington House, Piccadilly.) Mr. Paul Cadbury, Dr. Murdoch MacGregor, Dr. Catherine Wright: Problem Families.
OXFORD UNIVERSITY
5 P.M. (Radcliffe Infirmary.) Prof. William Doolin: Abraham Colles and His Contemporaries. (Litchfield lecture.)
MIDLAND MEDICAL SOCIETY, 36, Harborne Road, Edgbaston
8.15 P.M. Dr. Leslie Hill, Dr. D. L. Crombie, Mr. A. G. Timbrell Fisher, Dr. J. W. T. Patterson: Rheumatic Pain.

### Thursday, 21st

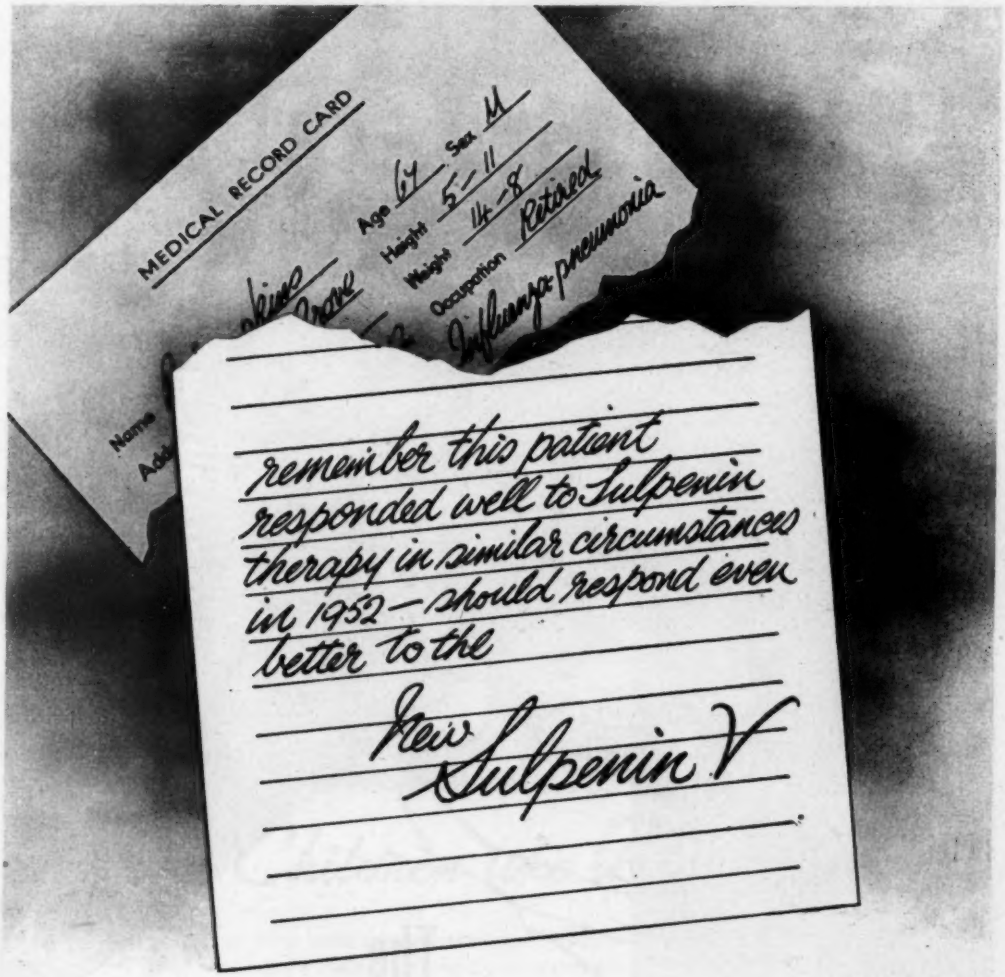
ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Dr. Sidney Thompson: Molluscum Sebaceum and its Surgical Significance. (Hunterian lecture.)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. J. H. Humphrey: Antibody Metabolism.
WEST LONDON MEDICO-CHIRURGICAL SOCIETY, West London Hospital, W.6
8.30 P.M. Dr. Macdonald Critchley: The Language of Gesture.
HYPNOTHERAPY GROUP
8 P.M. (1, Wimpole Street, W.1.) Dr. Oliver Garrod, Dr. A. W. Frankland, Dr. A. Denis Leigh: Asthma.
MANCHESTER MEDICAL SOCIETY
8 P.M. *Anæsthetics.* (Staff House, University of Manchester.) Dr. J. P. Payne: Influence of Carbon Dioxide on the Neuromuscular Blocking Activity of Relaxant Drugs.
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Prof. Ian Donald: Respiratory Phenomena in the Newborn.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Queen's College, Dundee.) Dr. T. F. Fox: The Art of the Article.

### Friday, 22nd

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Sir Wilfred Fish: An Enterprise in Dental Research. (Webb-Johnson lecture.)
ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS, 58, Queen Anne Street, W.1
5 P.M. Mr. Bethel Solomons: History of Infant Welfare. (William Meredith Fletcher Shaw lecture.)
ROYAL SOCIETY OF MEDICINE
8.15 P.M. *Obstetrics and Gynæcology.* Dr. G. F. Abercrombie, Mr. John Hamilton, Mr. John Peel, Mr. David Methuen: The Breech.
POSTGRADUATE MEDICAL SCHOOL
10 A.M. Dr. L. M. Franks: Hormones and Prostatic Growth.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, Gray's Inn Road, W.C.1
4.30 P.M. Miss Josephine Collier: Otolaryngology, a Synoptic Discipline.
MIDLAND CENTRE FOR NEUROSURGERY, Smethwick Hospital, Holly Lane, Smethwick, nr. Birmingham
8 P.M. Mr. Murray Falconer: Temporal Lobe Epilepsy.

### Saturday, 23rd

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
11.30 A.M. Prof. Gösta Dohlman (Lund): Experimental Studies on the Function of the Labyrinth.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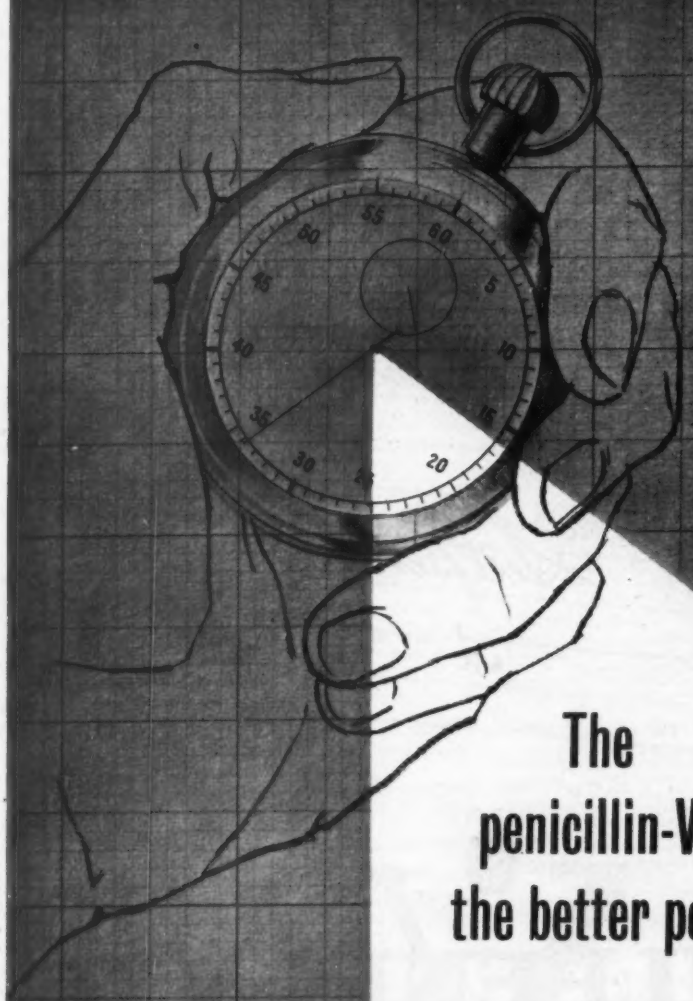

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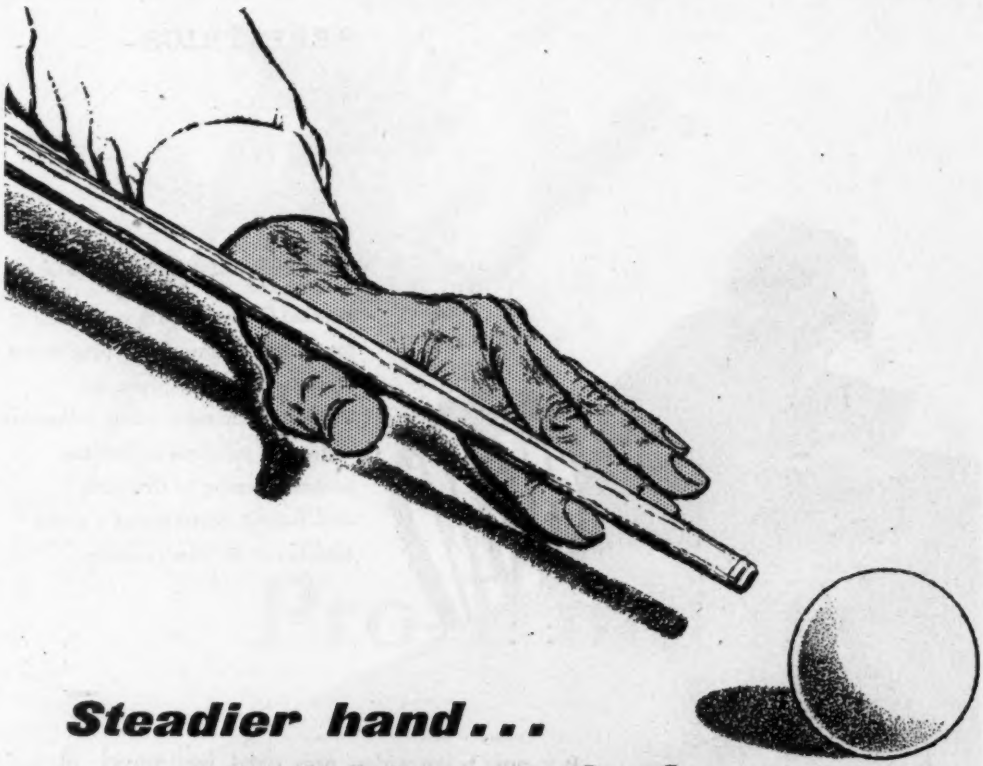

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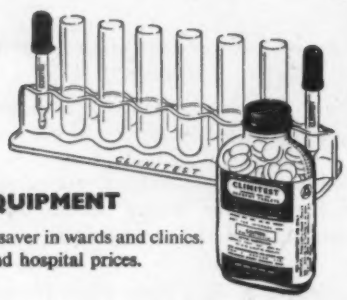


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(1954) 'Clinical Tests for Ketonuria', *'Lancet', April 17th, pp. 801/804*
(1954) '*Medicine Illustrated*', *May, p. 289*
(1954) '*Practical Clinical Biochemistry*', *Heinemann, p. 74*
(1954) 'Clinical Tests for Ketonuria', *'Lancet', July 10th, p. 95*

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## Academic and Educational

**PADDINGTON GROUP HOSPITAL MANAGEMENT COMMITTEE**
(THE TAVISTOCK CLINIC)

DISCUSSION GROUP SEMINAR ON PSYCHOLOGICAL PROBLEMS IN SPECIALIST AND HOSPITAL PRACTICE

It is planned to start a COURSE of 8 to 10 discussion meetings for a limited number of consultants and other senior medical hospital staff. Meetings will be held on TUESDAYS 7.30–9.30 P.M. Admission free.

Apply in writing for further particulars to Medical Director, Tavistock Clinic, 2, Beaumont-street, W.1, stating possible times for attending.

**GRESHAM COLLEGE, Basinghall-street, London, E.C.2**
Tel. MONarch 2433

4 LECTURES by Prof. J. L. D'SILVA, D.SC., M.R.C.P. (Gresham Professor in Physic), on "Nervous System" on MONDAY-THURSDAY, 18TH–21ST NOVEMBER.

The Lectures are free and begin at 5.30 P.M.

**IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY**

A COURSE of 8 LECTURES on "Microscopy" will be given by B. K. JOHNSON on TUESDAYS and THURSDAYS at 4 P.M. commencing TUESDAY, 28TH JANUARY, 1958.

This will be followed by a course of Practical Instruction, commencing 24th February, 1958, until 21st March.

Application for admission to either, or both of these courses should be made to the Registrar, Imperial College, Prince Consort-road, London, S.W.7.

**UNIVERSITY OF ST. ANDREWS**
QUEEN'S COLLEGE, DUNDEE

COX CHAIR OF ANATOMY

The University Court of the University of St. Andrews invites applications for the Cox Chair of Anatomy. The Professor will be a member of Queen's College, Dundee. The salary attached to the Chair is £3000 p.a. plus F.S.S.U. and Family Allowances. A grant towards the expenses of removal may be made.

Applications (30 copies), including the names of 3 referees, must be submitted by 28th February, 1958, to the undersigned, from whom further particulars may be obtained.

PATRICK CUMMING, Joint Clerk to the University Court.
Queen's College, Dundee. November, 1957.

**THE QUEEN'S UNIVERSITY OF BELFAST.** Applications are invited for a CIBA FELLOWSHIP in Biochemistry in the Department of Surgery. The applicant should hold an honours B.Sc. or its equivalent. Some knowledge of physiology is desirable. The Fellow will be required to work as a member of a team investigating endrocrinological problems related to surgery and will be encouraged to work for a higher degree. The appointment will be made for 2 years in the first instance. Salary £550–£600. F.S.S.U. and National Insurance contribution paid.

Applications should reach the Secretary of the University by 30th November, 1957.

**JERUSALEM, ISRAEL. ROTHSCHILD HADASSAH UNIVERSITY HOSPITAL.** Applications are invited from physicians of suitable academic status for the post of HEAD OF THE DEPARTMENT OF UROLOGY of the Rothschild Hadassah University Hospital in Jerusalem, with a view to candidature also for senior academic appointment in the Hebrew University Hadassah Medical School. The post is preferably a full-time one at an approximate gross salary of IL.670 per month, including cost-of-living and family allowances, with the right of limited consultant practice within the hospital; alternatively, a part-time appointment with the full right of private practice will be considered. Accommodation at a moderate rental will be made available to the successful candidate.

Inquiries and applications accompanied by curriculum vitæ, copies of publications and names of 3 references, should reach the Director General, Hadassah Medical Organisation, P.O.B. 499, Jerusalem, Israel, by 31st January, 1958.

**JERUSALEM, ISRAEL. ROTHSCHILD HADASSAH UNIVERSITY HOSPITAL.** Applications are invited for physicians of suitable academic status for the post of HEAD OF THE DEPARTMENT OF PLASTIC SURGERY of the Rothschild Hadassah University Hospital in Jerusalem, with a view to candidature also for senior academic appointment in the Hebrew University Hadassah Medical School. The post is preferably a full-time one at an approximate gross salary of IL.670 per month, including cost-of-living and family allowances, with the right of limited consultant practice within the hospital; alternatively, a part-time appointment with full right of private practice will be considered. Accommodation at a moderate rental will be made available to the successful candidate.

Inquiries and applications accompanied by curriculum vitæ, copies of publications and names of 3 references should reach the Director General, Hadassah Medical Organisation, P.O.B. 499, Jerusalem, Israel, by 31st January, 1958.

**MAKERERE COLLEGE. The University College of East AFRICA.** Applications are invited for LECTURESHIP IN PATHOLOGY. Salary scale £1446–£57–£1617–£60–£1737–£63–£1989 p.a., entry point determined by qualifications and experience. F.S.S.U. Child allowance £50 p.a. per child (maximum £150 p.a.). Passages for appointee and family (up to 4 adult passages) on appointment, termination and leave (3 months every 21 months). Rent according to quarters provided (£45–£84 p.a.) including basic furniture.

Detailed applications (6 copies), naming 3 referees, by 19th December, 1957, to Secretary, Inter-University Council for Higher Education Overseas, 29, Woburn-square, London, W.C.1, from whom further particulars may be obtained.

**NAPT SYMPOSIUM MEETINGS**

LUNG CARCINOMA. Chairman: N. LLOYD RUSBY, M.A., D.M., F.R.C.P. FRIDAY, 22ND NOVEMBER.

CARDIAC PROBLEMS FOR GENERAL PHYSICIANS. Chairman: K. SHIRLEY SMITH, B.SC., M.D., F.R.C.P. FRIDAY, 6TH DECEMBER.

Both meetings 3.30–6.30 P.M. in Great Hall, B.M.A. House, W.C.1. Tickets, including afternoon tea and sherry, 10s. each.

Details from NAPT, Tavistock House North, W.C.1.

**NAPT**

SYMPOSIUM ON CHRONIC BRONCHITIS, Edinburgh. WEDNESDAY, 20TH NOVEMBER, 3.30–6.30 P.M. Adam House.

Details from NAPT, 65, Castle-street, Edinburgh.

Tickets, including afternoon tea and sherry, 10s. each.

**NAPT**

A SCHOLARSHIP of £350 is offered to enable a British Chest Physician to study tuberculosis and other chest diseases in Canada for three months.

Applications to the Secretary-General, NAPT, Tavistock House North, Tavistock-square, London, W.C.1. Closing date 31st December, 1957.

## Hospital Services: Senior Appointments

**GUY'S HOSPITAL. The Board of Governors invite** applications for the appointment of CONSULTANT DENTAL SURGEON for attendance on 1 session at Guy's Hospital and 1 session at the Evelina Hospital per week. The appointment is of Consultant status and applicants should hold a registrable dental qualification and an additional higher qualification. The conditions of service will be in accordance with the terms and conditions of service of hospital dental staff.

Applications (1 copy), together with the names of 3 referees, should be lodged with the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 17th December, 1957. In accordance with Statutory Instrument No. 1259 of the National Health Service Regulations, canvassing members of the Board or Advisory Appointments Committee will lead to disqualification.

**SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD** requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at the Fountain Hospital, Tooting-grove, S.W.17 (800 Beds), to assist in clinical work, teaching and research. Applicants should preferably have special experience of mental deficiency or pædiatrics. Further particulars and arrangements for visiting hospital from the Physician-Superintendent.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 7th December, 1957.

**SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD** requires Part-time ASSISTANT OPHTHALMOLOGIST(S) (Senior Hospital Medical Officer grade) for sessions at the following London County Council Vision Clinics :

(*a*) St. Christopher's School Treatment Centre, 40A, York-road, S.W.11. (Tuesday A.M., or Wednesday A.M., or Thursday P.M., or Friday P.M., weekly.)

(*b*) Streatham School Treatment Centre, 55, Lewin-road, S.W.16. (Monday A.M., and P.M., weekly).

(*c*) Victoria Drive School Treatment Centre, 67, Victoria-drive, S.W.19. (Monday, Tuesday, Thursday, or Friday P.M., weekly.)

(*d*) St. Dunstan's Road School Treatment Centre, London, W.6. (Monday A.M. or Wednesday A.M., or Wednesday P.M., weekly.)

Candidates, who may apply for any or all of the above sessions, should be interested and experienced in children's work. Duties will be undertaken in collaboration with the Divisional Medical Officers of the London County Council. Successful candidate(s) will be required to take annual leave during the school vacations.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 7th December, 1957. Applicants may visit the various clinics by direct arrangement with the L.C.C. Divisional Medical Officers at 50–52, Fairfield-street, S.W.18 (Vandyke 2351), for Centres (*a*), (*b*), and (*c*), and at 133, Fulham Palace-road, W.6 (Riverside 8631) for (*d*).

**NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.**

Whole-time DEPUTY DIRECTOR (Senior Hospital Medical Officer grade) at Regional Blood Transfusion Centre (National Blood Transfusion Service) Crescent-drive, Brentwood, Essex. Residence in area a condition of appointment. Further particulars on application.

Part-time CONSULTANT RADIOLOGIST to Forest Group of hospitals (duties at Connaught, Chingford and Woodford Jubilee Hospitals) for 7 sessions a week. Further particulars on application.

Part-time CONSULTANT PÆDIATRICIAN to Barking Hospital, Upney-lane, Barking, Essex, for 1 session a week and 1 session a fortnight.

Applications (6 copies), stating post concerned, and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 14th December.

**NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.** CONSULTANT SURGEON, 7 half-days a week, Barnet General Hospital, Wellhouse-lane, Barnet (461 Beds). Successful candidate may be required to work also at other hospitals in the Barnet Group, and is required to live within easy reach of Barnet General Hospital, which may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, before 2nd December, 1957.

**BIRMINGHAM REGIONAL HOSPITAL BOARD.** Whole-time CONSULTANT RADIOLOGIST to Stafford Group of Hospitals. Duties mainly at Staffordshire General Infirmary and also at St. George's Hospital, Stafford. Wide experience specialty and higher qualification required.

Applications (15 copies), stating name, age, nationality, present and previous appointments, and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 16th December, 1957.

**BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS.** Applications are invited for the appointment of CONSULTANT ANÆSTHETIST on the basis of maximum part-time service.

Applications, giving the names of 3 referees, must be submitted on a form to be obtained from the Secretary to the Board of Governors, Queen Elizabeth Hospital, Birmingham, 15, and returned by Monday, 9th December, 1957.

**BRISTOL CLINICAL AREA. SOUTH-WESTERN REGIONAL HOSPITAL BOARD.** Applications are invited for the appointment of ASSISTANT PSYCHIATRIST to the Bristol Mental Hospital Group (Barrow and Fishponds Hospitals, Bristol Neurosis Centre, and Bristol Day Hospital). The appointment will be on a whole-time basis in the Senior Hospital Medical Officer grade. The successful candidate will work under the general direction of the Medical Superintendent of Bristol Mental Hospitals. An unfurnished house may be available.

Applications (12 copies), stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 30th November, 1957.

**BRISTOL. UNITED BRISTOL HOSPITALS (BRISTOL EYE HOSPITAL). SOUTH-WESTERN REGIONAL HOSPITAL BOARD.** The United Bristol Hospitals (which includes the Bristol Eye Hospital) and the South-Western Regional Hospital Board jointly invite applications for a post of CONSULTANT OPHTHALMIC SURGEON. Initially the appointment will be for 5 sessions in the Teaching Hospital and 1 session for the Regional Board in the Bristol Clinical Area. The terms and conditions of service recently negotiated between the Ministry and the Profession will apply to the appointment.

Applications, stating full Christian names, age and particulars of education, qualifications and experience, accompanied by 2 recent testimonials and the names of 2 referees, should be sent to the Secretary, Bristol Royal Infirmary, Bristol, 2, from whom further particulars can be obtained, not later than Monday, 16th December, 1957.

**NEWCASTLE REGIONAL HOSPITAL BOARD.** Assistant OPHTHALMOLOGIST (Senior Hospital Medical Officer) whole-time, or maximum part-time for 9 notional half-days per week, for Sunderland and Hartlepools Groups of hospitals—main hospitals Sunderland Eye Infirmary (60 Beds), Sunderland Royal Infirmary (300 Beds), Sunderland General Hospital (444 Beds), General Hospital, West Hartlepool (468 Beds), Hartlepools Hospital (112 Beds). Population served: Sunderland 362,630, Hartlepools 132,110. Further particulars from Senior Ophthalmic Surgeon, Clinic No. 1. Sunderland Eye Infirmary, Sunderland.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

**NEWCASTLE REGIONAL HOSPITAL BOARD.** Senior CONSULTANT PHYSICIAN (Whole-time or maximum part-time) required for the Sunderland Group of hospitals. The Physician appointed should have had special experience in geriatrics, and will be asked to take charge of the Geriatric Unit in this Group. The number of beds is 506, primarily in the Sunderland General Hospital (217 Beds). Other beds are in Ryhope General Hospital (96), Leeholme Hospital, Easington (161) and Boldon Hospital (32). A small number of beds in acute medical wards will also be allocated to the Physician to be appointed, probably in Ryhope General Hospital. A Research Unit is attached to the Geriatric Department, and it is hoped that the person appointed will continue to develop the research into geriatric problems which has been conducted in the past. Further particulars available from Senior Administrative Medical Officer. Candidates may visit the hospitals by arrangement.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

**SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD** requires Whole-time ASSISTANT CHILD PSYCHIATRIST (Senior Hospital Medical Officer grade) to work under Consultant in the Hampshire Child Guidance Service. Successful candidate will be required to act as Psychiatrist at certain of the Child Guidance Clinics provided by the Hampshire Education Committee, predominantly in the southern part of the County, and at the Approved School and Remand Homes in Winchester.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 7th December, 1957. Applicants may visit Clinics by arrangement with County Medical Officer of Hampshire County Council.

**SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD** requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Herrison Hospital, Dorchester, Dorset (1050 Beds). Candidates should possess D.P.M. and should have had wide experience in psychiatry.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 7th December, 1957. Applicants may visit Hospital by arrangement with the Medical Superintendent.

**LEEDS REGIONAL HOSPITAL BOARD.**

CONSULTANT in Anæsthetics (maximum part-time sessions). Hospitals in the East Riding of Yorkshire—mainly at Westwood Hospital, Beverley. 1 session at Hull Royal Infirmary. Person appointed to reside in Beverley.

Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer scale), Broadgate Hospital, Beverley, and associated clinics at Beverley, Driffield, and Hull. Married accommodation may be available. Candidates should normally hold a D.P.M. but applications will also be considered from candidates without previous experience in psychiatry who hold a higher medical qualification, have had wide experience in general medicine in the Senior Registrar grade and intend to obtain a D.P.M. and specialise in psychiatry.

Whole-time ASSISTANT RADIOTHERAPIST (Senior Hospital Medical Officer scale) in the Regional Radiotherapy Service for duties mainly at the Hull Royal Infirmary. Relief duties as may be required at other radiotherapy centres in the region. The person appointed to work under the supervision of the Consultant in Radiotherapy and to reside in the Hull area.

Applications (12 copies), stating age, qualications and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 10th December, 1957.

**SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD.** Whole-time PSYCHIATRIST (Senior Hospital Medical Officer grade) at East Lothian Mental Hospital, Haddington (235 Beds). The Hospital is under the charge of a Consultant Psychiatrist who is Medical Superintendent of both Haddington and Rosslynlee Mental Hospitals.

Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

**SHEFFIELD REGIONAL HOSPITAL BOARD.** Whole-time NON-RESIDENT SENIOR CASUALTY OFFICER required at the Beckett Hospital, Barnsley. Salary scale, £1653 15s.–£52 10s.–£2126 5s. p.a. Tenure for a period not exceeding 4 years.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 14th December, 1957.

**SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.** Applications are invited for an appointment as CONSULTANT PATHOLOGIST to the Hastings Group of hospitals. Choice of whole-time service or part-time service for the maximum of 9 notional half-days will be offered. Candidates must have had wide experience in pathology and a higher University degree or membership of a Royal College of Physicians is desirable; special experience in biochemistry would be an advantage. Applicants may visit the hospitals concerned.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to: The Secretary, Advisory Appointments Committee, South-East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 30th November, 1957.

**AUSTRALIA. ROCKHAMPTON HOSPITAL, Queensland.** Applications are invited for appointment as Part-time PHYSICIAN at the Rockhampton Base Hospital. 4 2-hour sessions per week. Salary at the rate of £907 p.a. Rockhampton has a population of 42,000 and is the centre of district of 90,000 population. Further particulars of the position and opportunity for private practice will be forwarded upon request.

Applications should be addressed to the Secretary, Rockhampton Hospitals Board, Rockhampton. Applications close on 31st December, 1957.

## Hospital Services: Junior Appointments

**ALL SAINTS' HOSPITAL (Westminster Hospital Teaching Group),** Austral-street, West-square, London, S.E.11. Applications are invited for the post of SURGICAL REGISTRAR (urological) for 1 year in the first instance, from 1st January, 1958, subject to the usual terms and conditions of service of hospital medical and dental staffs. The post is primarily for the Urological Department, but some general surgery is also included; it offers time for postgraduate study and there is access to clinical material throughout the Group.

Applications (7 copies), with the names of 2 referees, should reach the Secretary at the above address not later than 23rd November, 1957.

**BOLINGBROKE HOSPITAL, Wandsworth Common,** S.W.11. HOUSE SURGEONS (2), resident. Vacant 1st January, 1958, and 10th January, 1958. Open to registered practitioners and pre-registration candidates.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 26th November, 1957.

**CITY OF LONDON MATERNITY HOSPITAL, Hanley-road,** London, N.4. OBSTETRIC HOUSE SURGEONS (2). Both posts recognised for D.Obst.R.C.O.G. and M.R.C.O.G., vacant 3rd December and 22nd December.

Application forms obtainable from Hospital Secretary, returnable by 22nd November.

**COLINDALE HOSPITAL, Colindale-avenue, London,** N.W.9. (300 Beds.) **NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.** Whole-time SURGICAL REGISTRAR, resident or non-resident, required at above Hospital. F.R.C.S. and previous experience an advantage. Post vacant 1st January, 1958. Work covers surgical treatment of pulmonary, orthopædic, urinary, and tuberculous and non-tuberculous chest diseases. The Hospital is situated within easy reach of central London and may be visited by arrangement with Physician-Superintendent.

Application forms obtainable from and returnable to Group Secretary, Hendon Group Hospital Management Committee, Edgware General Hospital, Edgware, Middlesex, by 26th November, 1957.

**BARNES HOSPITAL, South Worple-way, London, S.W.14.** (114 Beds.) KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical practitioners for the appointment of 1 or 2 CLINICAL ASSISTANTS to the Geriatrician at the above Hospital for the equivalent of 2 notional half-days per week (including emergency cover rota with Geriatrician). Salary will be at the rate of £183 15s. p.a. per weekly notional half-day. The appointment is for 1 year in the first instance, subject to review.

Applications, stating age, qualifications, experience and names of 2 referees, should be sent within 14 days of the appearance of this advertisement to the Group Secretary, Kingston Group Hospital Management Committee, 35, Coombe-road, Kingston-on-Thames.

**CAMBERWELL HOSPITALS MANAGEMENT COMMITTEE.** Applications invited for appointment to the undermentioned recognised pre-registration posts vacant from 1st January, 1958:—

(1) **At Dulwich Hospital** (in association with King's College Hospital Medical School for teaching purposes) East Dulwich-grove, S.E.22

HOUSE OFFICER (general medical duties)—3 positions.
HOUSE OFFICER (general surgical duties)—3 positions.

(2) **At St. Giles' Hospital, Camberwell, S.E.5**

HOUSE OFFICER (general medical duties)—1 position.
HOUSE OFFICER (general surgical duties)—1 position.
HOUSE OFFICER (orthopædic duties)—1 position.

Applications, giving age, qualifications and details of previous post (if any), with copy testimonials or names of 2 referees, to be sent to the Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, East Dulwich-grove, S.E.22, not later than 25th November, 1957.

**EASTMAN DENTAL HOSPITAL AND INSTITUTE OF DENTAL SURGERY** (UNIVERSITY OF LONDON), Gray's Inn-road, London, W.C.1. Applications are invited for the full time post of ANÆSTHETIST in the grade of Registrar. Remuneration and conditions of service in accordance with national scales.

Application forms should be obtained from the Director.

**ELIZABETH GARRETT ANDERSON HOSPITAL,** Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from pre-registration and registered Women medical practitioners for the post of FIRST HOUSE PHYSICIAN for Medicine and Prediatrics, to become vacant 1st January, 1958. Appointment for 6 months. Salary in accordance with Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 20th November, 1957.

**ELIZABETH GARRETT ANDERSON HOSPITAL,** Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from pre-registration and registered Women medical practitioners for the post of SECOND HOUSE PHYSICIAN. Appointment for 6 months from 1st January, 1958. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 20th November, 1957.

**ELIZABETH GARRETT ANDERSON HOSPITAL,** Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from pre-registration and registered Women medical practitioners for the post of FIRST HOUSE SURGEON, with charge of General Surgical Beds. Appointment for 6 months from 1st January, 1958. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 20th November, 1957.

**ELIZABETH GARRETT ANDERSON HOSPITAL,** Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from pre-registration and registered Women medical practitioners for the post of SECOND HOUSE SURGEON. Appointment for 6 months, from 1st January, 1958. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 20th November, 1957.

**ELIZABETH GARRETT ANDERSON HOSPITAL,** Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from pre-registration and registered women medical practitioners for the post of OBSTETRIC HOUSE SURGEON (recognised for the M.R.C.O.G.). Duties to commence 1st January, 1958. Appointment for 6 months. Salary in accordance with Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, to be sent to The Secretary, Elizabeth Garrett Anderson Hospital, by 20th November, 1957.

**HACKNEY HOSPITAL, London, E.9.** (General—841 Beds.) Applications for the 6-months-Resident-House-Officer appointments of :—

(*a*) CASUALTY OFFICER AND HOUSE SURGEON (E.N.T.), now vacant;
(*b*) CASUALTY OFFICER AND HOUSE PHYSICIAN, Skin Department, now vacant,

should be sent immediately to Secretary, above address, quoting Casualty Officer (*a*) or (*b*).

**LAMBETH GROUP HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited from registered medical practitioners (Women) for the post of SENIOR HOUSE OFFICER in Anæsthetics at the South London and South Western Hospitals (joint appointment). Vacant 1st February, 1958.

Application form from the Secretary, South London Hospital for Women, Clapham Common, S.W.4.

**LAMBETH HOSPITAL, Brook-drive, S.E.11. Locum** ANÆSTHETIC REGISTRAR required from 23rd November to 13th December inclusive.

Apply to Secretary (Tel. : RELiance 3804, Ext. 18).

**LAMBETH HOSPITAL, Brook-drive, S.E.11. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD.** Applications are invited from registered medical practitioners for the post of RESIDENT OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR, which will become vacant in January, 1958. The appointment is normally for 2 years, subject to annual review. The post is recognised for the M.R.C.O.G., and includes some teaching of medical students from St. Thomas's Hospital. Candidates may visit the Hospital.

Forms of application obtainable from the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, should be returned by 30th November, 1957.

**LAMBETH HOSPITAL, Kennington, S.E.11.** Applications are invited from pre-registration and registered Medical Practitioners for the post of RESIDENT HOUSE SURGEON in the Obstetric and Gynæcological Unit. The appointment is for 6 months from 1st January, 1958. It would be convenient if the successful candidate could carry out a fortnight's locum duty, starting from 18th December, 1957. Hospital recognised for the M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms from the Secretary.

**LONDON CHEST HOSPITAL (Country Branch). HOSPITALS FOR DISEASES OF THE CHEST.** REGISTRAR in Clinical Pathology (Registrar grade). A vacancy occurs 1st January, 1958, at the Country Branch, near Letchworth. The appointment is a whole-time one and will be for 1 year in the first instance, and the holder may be resident or non-resident.

Applications, stating age, qualifications, with dates, and previous experience, together with copies of 3 testimonials, should be forwarded at once to the undersigned.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

**LONDON JEWISH HOSPITAL, Stepney Green, E.1.** (130 Beds.) HOUSE PHYSICIAN (pre- or post-registration) required for 6 months. Post vacant 11th December, 1957.

Applications, stating age, experience, &c., and copies of not more than 3 testimonials, to be sent to the Hospital Secretary not later than 22nd November, 1957.

**KING EDWARD MEMORIAL HOSPITAL, Ealing. Senior** HOUSE OFFICER (anæsthetics) for duties at King Edward Memorial Hospital and Associate Hospitals. Resident. Vacant 8th January. Resident Registrar Anæsthetist employed. Post recognised for D.A. and F.F.A.R.C.S. examinations.

Apply, stating age, nationality, qualifications and experience, with copies of up to 3 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 28th November.

**MIDDLESEX HOSPITAL, W.1. Applications invited for** post of ASSISTANT in the Department of Cardiology with status of Senior Medical Registrar. Appointment will also involve duties in the Thoracic Surgical Unit. Previous cardiological training essential.

Forms of application obtainable from the Deputy Superintendent should be returned, naming 2 referees, by 7th December.

**MIDDLESEX HOSPITAL, W.1. Applications invited for** post of REGISTRAR in Anæsthetics, vacant 1st January.

Rules and application form obtainable from Deputy Superintendent should be returned, naming 2 referees, by 7th December.

**MIDDLESEX HOSPITAL, W.1. Applications invited for** posts of :—

SENIOR HOUSE OFFICER in Anæsthetics,
JUNIOR RESIDENT ASSISTANT ANÆSTHETIST (graded as House Officer),

vacant 1st February.

Forms of application obtainable from Deputy Superintendent should be returned, naming 2 referees, by 7th December.

**NATIONAL HOSPITALS FOR NERVOUS DISEASES.** Applications are invited from registered medical practitioners for the appointment of SENIOR RESIDENT HOUSE PHYSICIAN at The National Hospital, Queen-square, W.C.1, to commence 1st February, 1958. This post carries the grade of Registrar. The appointment will be for 1 year and will be renewed in exceptional circumstances.

Applications, with names of 3 referees, to be sent to the undersigned not later than 29th November, 1957.

H. EWART MITCHELL,
Secretary to the Board of Governors.
The National Hospitals for Nervous Diseases,
Queen-square, W.C.1.

**NATIONAL HOSPITALS FOR NERVOUS DISEASES.** Applications are invited from registered medical practitioners for the appointment of NON-RESIDENT HOUSE PHYSICIAN at The National Hospital, Queen-square, W.C.1, to commence 1st February, 1958. There are 2 vacancies. These posts carry the grade of Senior House Officer. The appointments will be for 6 months.

Applications, with names of 3 referees, to be sent to the undersigned not later than 29th November, 1957.

H. EWART MITCHELL,
Secretary to the Board of Governors.
The National Hospitals for Nervous Diseases,
Queen-square, W.C.1.

**NORTH MIDDLESEX HOSPITAL, London, N.18. Applications** are invited for the post of resident HOUSE PHYSICIAN (general medicine). 6 months' appointment, starting on 1st January, 1958. Approved pre-registration post (first or second).

Applications, giving full particulars, together with copies of recent testimonials, should reach the Secretary of the Hospital by 27th November.

**NORTH MIDDLESEX HOSPITAL, London, N.18. Applications** are invited from pre- and post-registration candidates for the posts (2) of RESIDENT HOUSE SURGEONS (general with some genito-urinary surgery). 6 months' appointments, vacant 1st January, 1958. Both posts recognised for F.R.C.S.

Applications, giving full particulars, together with copies of recent testimonials, should reach the Secretary of the Hospital by 27th November.

**NORTH MIDDLESEX HOSPITAL, London, N.18.** Applications are invited for the post of ADMISSIONS OFFICER (Senior House Officer grade). 6 months' appointment; non-resident; vacant 1st January, 1958. This is a busy post in a new department. The evenings and weekends (from 1 P.M. Saturday) are free.

Applications, giving full particulars, with copies of recent testimonials and/or names of 2 referees, should reach the Secretary of the Hospital not later than 27th November.

**PRINCESS BEATRICE HOSPITAL, Earls Court, London, S.W.5.** Applications are invited from fully registered medical practitioners for the post of OBSTETRIC HOUSE SURGEON with gynæcology and some general surgery. Senior House Officer grade. Resident. Vacancy mid-December.

Applications, with 3 testimonials, to the House-Governor, not later than 25th November, 1957.

**QUEEN ELIZABETH HOSPITAL FOR CHILDREN** MANAGEMENT COMMITTEE, Hackney-road, E.2, Shadwell, E.1, and BANSTEAD WOOD, SURREY. SENIOR RESIDENT MEDICAL OFFICER (Male or Female), graded as Senior House Officer. Senior of 7 House Officers, in a hospital engaged in postgraduate and undergraduate teaching. Previous paediatric experience essential. Post vacant 1st February, 1958, at Hackney-road branch. Appointment for 1 year.

Application forms (obtainable from the Secretary at Hackney-road) should be returned with copies of 3 testimonials not later than 27th November, 1957.

**QUEEN MARY'S HOSPITAL FOR THE EAST END,** Stratford, E.15. HOUSE PHYSICIAN (pre-registration) required for 6 months, commencing 2nd January, 1958.

Applications, with copies of recent testimonials, to Hospital Secretary by 22nd November, 1957.

**QUEEN MARY'S HOSPITAL FOR THE EAST END,** Stratford, E.15. SENIOR HOUSE SURGEON (Senior House Officer grade) required for 6 months, commencing 5th December, 1957. Post recognised for F.R.C.S.

Applications, with the names of 3 referees, to Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, by 22nd November, 1957.

**QUEEN MARY'S HOSPITAL FOR THE EAST END,** Stratford, E.15. HOUSE SURGEON (pre-registration) required for 6 months, commencing 2nd January, 1958.

Applications, with copies of recent testimonials, to Hospital Secretary by 22nd November, 1957.

**ROYAL FREE HOSPITAL AND NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.** Applications are invited for the whole-time appointment of SENIOR REGISTRAR in Psychiatry with 6 sessions at the Royal Free Hospital, Gray's Inn-road, London, W.C.1, and 5 sessions at the Friern Hospital, New Southgate, London, N.11.

Applications, stating age, qualifications and experience, together with the names and addresses of 3 referees, to the Secretary to the Board, Royal Free Hospital, Gray's Inn-road, W.C.1, by 29th November, 1957.

**ROYAL FREE HOSPITAL.** Applications are invited from registered medical practitioners for the post of SENIOR CASUALTY OFFICER at the Royal Free Hospital, Gray's Inn-road, W.C.1. The appointment is full-time, resident for 6 months, duties to commence 1st January, 1958. Salary and conditions of service in accordance with the scale laid down by the Ministry of Health for Senior Health Officers.

Application forms may be obtained from the Hospital Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 28th November, 1957.

**ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL, AND INSTITUTE OF LARYNGOLOGY AND OTOLOGY,** Gray's Inn-road, W.C.1, and Golden-square, W.1. Applications are invited for a post of SENIOR REGISTRAR, with effect from 1st January, 1958. The appointment will be for an initial period of 1 year, subject to annual re-election thereafter up to a maximum permissible term in this grade, and otherwise in accordance with the terms and conditions of service in the National Health Service. Applicants must have had considerable experience in general surgery and in this specialty and hold a higher surgical qualification.

Applications should give full information as to qualifications and experience, and the names of 2 referees, and be sent in duplicate to the House Governor before 28th November.

**ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL,** Gray's Inn-road, W.C.1, and Golden-square, W.1. RESIDENT HOUSE SURGEON (post-registration post). Applications are invited for a 6 months' appointment as from 1st January, 1958, with salary and conditions as laid down for House Officers in the terms and conditions of service in the National Health Service.

Applications, stating age, qualifications, full details of previous experience (particularly in this specialty), with copies of 1–3 recent testimonials, should be sent to the House Governor without delay.

**ROYAL NORTHERN HOSPITAL, Holloway, N.7.** Applications are invited for the post of HOUSE SURGEON, vacant 18th December, 1957. Preference given to pre-registration candidates. Recognised for F.R.C.S.

Applications, with copies of recent testimonials, to be sent to the Hospital Secretary by 26th November, 1957.

**ST. GEORGE'S HOSPITAL, S.W.1.** Applications are invited for the post of SENIOR REGISTRAR to the Department of Psychiatry. The inpatient work of the Department is at the Atkinson Morley's Hospital, and the outpatient work at St. George's Hospital. The appointment is for 1 year in the first instance, and the successful candidate will be required to take up duty on 1st February, 1958.

Applications, stating age, education, qualifications, experience, and the names of 2 referees, should reach the undersigned not later than 14th December, 1957.

P. H. CONSTABLE, House Governor.

**ST. GEORGE'S HOSPITAL, S.W.1. Winchester and SOUTHAMPTON GROUPS OF HOSPITALS.** Applications are invited for the post of REGISTRAR to the Department of Paediatrics. The successful candidate will work jointly between St. George's Hospital Children's Department at the Victoria Hospital for Children and the Winchester and Southampton Groups of hospitals. Candidates should have had good experience of work in a Children's Hospital and should hold the D.C.H. Membership of the Royal College of Physicians would be an advantage. The appointment will be for 1 year in the first instance and the successful candidate will be required to take up duty on 1st March, 1958.

Applications, stating age, education, qualifications and experience, together with the names of 2 referees, should reach the undersigned not later than Saturday, 7th December, 1957.

P. H. CONSTABLE, House Governor.

St. George's Hospital.

**SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN,** Clapham Common, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered Women medical practitioners for the post of ANÆSTHETIC REGISTRAR (either resident or prepared to live within 20 minutes of the hospital). D.A. desirable but not essential. Post recognised for D.A. The appointment is normally for 2 years, but subject to review at the end of 1 year, and will be vacant on 1st January, 1958. Canvassing will disqualify but candidates may visit the hospital by arrangement.

Forms of application from the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to be returned by 30th November, 1957.

**ST. JAMES' HOSPITAL, Balham, London, S.W.12. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD.** Part-time REGISTRAR (7 sessions per week) required for Ophthalmic Unit (18–20 Beds and Outpatient Clinics). Resident or non-resident. Immediate vacancy on account of illness.

Application forms obtainable from Group Secretary, Wandsworth Hospital Group, at above address.

**ST. JAMES' HOSPITAL, Balham, London, S.W.12. Senior** HOUSE OFFICER (orthopædic and trauma). Post recognised for F.R.C.S. Vacant 11th December.

Applications, stating age, qualifications, experience, and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address by 27th November.

**ST. MARY'S HOSPITAL, Paddington, W.2. Casualty** SURGEON (non-resident) required for a first period of 6 months with effect from 1st January, 1958. Remuneration to be at Senior House Officer rates. Candidates must have held an appointment as House Surgeon at this Hospital or at another hospital approved by the Board of Governors.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 3rd December, 1957.

**ST. MARY'S HOSPITAL, W.2. Resident Anæsthetist** required with effect from 1st January, 1958. The appointment is for a first period of 6 months; remuneration to be at Senior House Officer rates.

Applications, stating nationality, date of birth, permanent address, qualifications with dates; details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 30th November, 1957.

**ST. NICHOLAS HOSPITAL, Plumstead, S.E.18.** SENIOR HOUSE OFFICER (Casualty Department). Vacant 27th November. Recognised for F.R.C.S. 6-month resident appointment and may then be renewed for a further period.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

**ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS.** RESIDENT SURGICAL OFFICER (Registrar grade) required for St. Philip's Hospital on 1st February, 1958. Appointment for 6 months with opportunity for extension. Work includes medical urology and opportunity for research.

Apply in writing (12 copies), and names of 2 referees, to the House Governor, St. Peter's Hospital, Henrietta-street, W.C.2. Closing date 7th December, 1957.

**ST. THOMAS'S HOSPITAL, London, S.E.1.** Applications are invited from fully registered medical practitioners for the following resident appointments:—

SENIOR MEDICAL CASUALTY OFFICER AND RESIDENT PATHOLOGIST (Senior House Officer grade).

SENIOR SURGICAL CASUALTY OFFICER (Senior House Officer grade).

SENIOR HOUSE OFFICER or HOUSE OFFICER to the Thoracic Surgical Unit (grade according to qualifications and experience).

HOUSE PHYSICIAN to the Children's Department.

HOUSE PHYSICIAN to the Department of Psychological Medicine.

HOUSE PHYSICIAN to the Departments of Neurology and Thoracic Medicine.

All for 6 months from 11th February, 1958.

Applications, naming 2 referees, to Clerk of the Governors, by 29th November, 1957.

**ST. THOMAS'S HOSPITAL, S.E.1, and the SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD** (joint appointment). Whole-time SENIOR MEDICAL REGISTRAR at St. Thomas's Hospital and the Southampton Group of hospitals for 1 year in the first instance from 15th March, 1958. Subject to annual reappointment, the successful candidate will be required to spend about a year at Southampton, the remainder of his time being spent at St. Thomas's Hospital.

Applications (6 copies), naming 2 referees, to Clerk of the Governors, by 6th December, 1957.

**WANSTEAD HOSPITAL, Harmon Hill, E.11. (191 Beds.)** Applications are invited for the post of OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEON, vacant 9th December, 1957. The appointment is recognised for the D.Obst.R.C.O.G.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

**WANSTEAD HOSPITAL, Harmon Hill, London, E.11.** (191 Beds.) HOUSE SURGEON required post vacant 24th December, 1957. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

**WEST END HOSPITAL FOR NEUROLOGY AND** NEUROSURGERY, 91, Dean-street, W.1. Applications are invited for the post of SENIOR HOUSE PHYSICIAN (organic neurology), commencing 1st January, 1958.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, to be forwarded to the Hospital Secretary by 30th November.

**WHIPPS CROSS HOSPITAL, London, E.11. Leytonstone** NO. 10 HOSPITAL GROUP. Applications are invited for the post of HOUSE PHYSICIAN (pre- or post-registration), general medicine, at above Hospital. Post vacant now.

Application forms obtainable from and returnable to the Hospital Secretary by 25th November, 1957.

**WHIPPS CROSS HOSPITAL, London, E.11. Applications** are invited for the following posts which become vacant 1st January, 1958:—

Pre-registration HOUSE PHYSICIAN (2 posts), general medicine.

Pre-registration HOUSE SURGEON (3 posts), general surgery.

Pre-registration HOUSE SURGEON, Gynæcology and Urology Departments.

Application forms obtainable from and returnable to the Hospital Secretary by 25th November, 1957.

**WILLESDEN GENERAL HOSPITAL, Harlesden-road,** N.W.10. Locum ANÆSTHETIC REGISTRAR required, 2 months or longer.

Apply Hospital Secretary.

**WHITTINGTON HOSPITAL, London, N.19. Applications** are invited for the post of post-registration HOUSE PHYSICIAN (neurosurgical). Vacant 16th December, 1957. Post recognised for M.D.(Lond.).

Application forms obtainable from Group Secretary, 46, Cholmeley-park, London, N.6 (ARC 3070, Ext. 527), and returnable to the Medical Superintendent, Whittington Hospital, N.19, by 25th November, 1957.

**WOOLWICH GROUP HOSPITAL MANAGEMENT COM-**MITTEE. HOUSE PHYSICIANS. 5 posts vacant 1st January, 3 at Brook General Hospital, Woolwich, 2 at St. Nicholas Hospital, Plumstead. All posts approved for pre-registration service.

Applications to Group Secretary, Memorial Hospital, Woolwich, S.E.18, not later than 30th November.

**WOOLWICH GROUP HOSPITAL MANAGEMENT COM-**MITTEE. HOUSE SURGEONS. 5 posts vacant 1st January, 3 at Memorial Hospital, Woolwich, 2 at St. Nicholas Hospital, Plumstead. All recognised for F.R.C.S., and approved for pre-registration service.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

**ALTON GENERAL HOSPITAL, Alton. (136 Beds—Acute** general.) RESIDENT HOUSE OFFICER required for general surgical duties. Post suitable for pre-registration candidates. Vacant early December, 1957. Recognised for F.R.C.S. 6-month appointment.

Applications and copies of testimonials to be sent to the Hospital Secretary by 3rd December.

**ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.)** STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE SURGEON for general surgical duties. 6 months' appointment, vacant in early December, 1957. Preference given to pre-registration candidates.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital.

**ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGE-**MENT COMMITTEE. HOUSE SURGEON required at Ashton-under-Lyne General Hospital. Preference will be given to pre-registration applicants. Recognised for F.R.C.S. (Eng.).

Applications, with copies of 2 testimonials, to Group Secretary, General Hospital, Ashton-under-Lyne.

**AYLESBURY. ROYAL BUCKINGHAMSHIRE HOS-**PITAL. HOUSE OFFICER (accident and orthopædic and children's general surgery). Pre-registration post, but registered practitioners invited to apply. Recognised for F.R.C.S.

Apply, with copies of 2 recent testimonials, to Secretary-Superintendent.

**AYRSHIRE HOSPITALS. Junior Hospital Medical Officer** (obstetrics and gynæcology), vacant 1st December. Based on Ayrshire Central Hospital. Offers wide experience obstetrics and gynæcology under consultant supervision and study time for M.R.C.O.G.

Apply immediately Area Medical Superintendent, 1, Hill-street, Kilmarnock.

**BEDFORD GENERAL HOSPITAL. (436 Beds.) 2 House** SURGEONS required. Pre- or post-registration; recognised for F.R.C.S. One vacant now, one end of November. Posts offer exceptional opportunities for general experience in busy acute surgical units.

Inquiries and applications, with copies of 2 recent testimonials, to be sent immediately to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

**BEDFORD GENERAL HOSPITAL. (436 Beds.) Ortho-**PÆDIC HOUSE SURGEON required. Vacant now. Pre- or post-registration; recognised for F.R.C.S. Post offers wide experience in a busy specialist orthopædic and traumatic unit.

Inquiries and applications, with copies of 2 recent testimonials, to be sent immediately to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

**BEDFORD GENERAL HOSPITAL. (436 Beds.) 2 Resi-**DENT HOUSE PHYSICIANS (pre-registration) required end November.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

**BEDFORD GENERAL HOSPITAL. (436 Beds.) North** WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required for busy acute Orthopædic and Traumatic Department at above Hospital. Previous orthopædic experience desirable. Candidates may visit the Hospital by appointment with the Group Secretary.

Application forms obtainable from and returnable to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 9th December, 1957.

**BARNSTAPLE. NORTH DEVON INFIRMARY (Central** Group Hospital of 105 Beds). SENIOR HOUSE SURGEON. Post vacant 13th January, 1958, for 1 year. Salary £819 10s. p.a. Furnished flat available for rental.

Applications, with customary details, to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

**BARNSTAPLE. NORTH DEVON INFIRMARY. (105** Beds.) HOUSE SURGEON (pre-registration); vacant now. The Hospital serves a wide area of pleasant countryside and the post affords good opportunity to study excellent clinical material.

Apply to Group Secretary, 19, Alexandra-road, Barnstaple.

**BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL.** (229 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer grading according to experience).

Apply Group Secretary.

**BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL.** (229 acute beds.) ORTHOPÆDIC HOUSE SURGEON (first, second or third post), vacant now. Offers good opportunity for general experience in busy acute general hospital. Approved pre-registration post. Fully registered practitioners may apply. Recognised for F.R.C.S.

Apply Group Secretary.

**BIRMINGHAM ACCIDENT HOSPITAL, Bath-row,** BIRMINGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEONS (resident). Vacant January/February. Hospital largest traumatic unit in country and treats over 50,000 new patients each year. Recognised for purpose of casualty by R.C.S. (Eng.). Teaching programme by consultant staff. 6-month appointment, some of which may be spent in 42-bedded Medical Research Council's Burns Unit.

Apply, naming 2 referees, to Administrator.

**BIRMINGHAM, 9. LITTLE BROMWICH GENERAL** HOSPITAL. RESIDENT MEDICAL OFFICER in Infectious Diseases (Senior House Officer grade). Hospital serves a wide area and gives opportunity for the study of infectious diseases, and has a poliomyelitis respiratory unit. Part of the hospital is being developed as a general hospital, where further experience can be gained.

Apply, Physician-Superintendent with 2 testimonials.

**BIRMINGHAM REGIONAL HOSPITAL BOARD.**

**1. Coventry No. 20 Group. Coventry and Warwick-shire Hospital, Coventry**

(a) REGISTRAR (anæsthetics) for Coventry and Warwickshire and Guison Hospitals. Experience specialty essential. Recognised F.F.A. R.C.S. Resident.

(b) REGISTRAR (pathology) for general duties at Nuneaton Hospitals and the Group Laboratory (recognised D.Path.). Non-resident.

**2. Birmingham (Dudley Road) Group, Dudley-road Hospital, Birmingham, 18**

REGISTRAR (pathology), non-resident, for Dudley Road Hospital (780 Beds). Recognised for Dip.Path. Post offers wide experience in all branches.

**3. Wolverhampton Group. The Royal Hospital, Wolverhampton**

REGISTRAR (ophthalmology) for Wolverhampton and Midland Counties Eye Infirmary. Experience in specialty essential, possession of D.O. preferable. Opportunities for wide clinical experience and studying. Married accommodation may shortly be available.

Application forms from Group Secretaries, to be returned by 25th November, 1957.

**BIRMINGHAM. THE UNITED BIRMINGHAM HOS-**PITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the post of RESIDENT MEDICAL OFFICER, second of 2 (Senior House Officer grade), vacant 1st January, 1958, for 1 year. Main duty to take charge of Infants Block (66 Cots). Valuable opportunity for further study of disease of infancy, some previous experience of which is desirable. M.R.C.P. preferred.

Forms of application available from the House Governor and should be returned to him by 30th November, 1957.

G. A. PHALP, Secretary to the Board of Governors.

**BIRMINGHAM. UNITED BIRMINGHAM HOSPITALS.** THE BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN, Showell Green-lane, SPARKHILL, BIRMINGHAM, 11. Applications are invited from registered medical practitioners for the post of RESIDENT GYNÆCOLOGICAL HOUSE SURGEON for duty with the Professorial Unit as soon as possible. The appointment is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms obtainable from the House Governor at the above address, to be returned not later than 27th November, 1957.

**BIRMINGHAM, 29. SELLY OAK HOSPITAL.** Senior HOUSE OFFICER (resident) E.N.T. Department. (42 Beds.)
Applications, giving age, qualifications and experience, to the Medical Superintendent.

**BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL.** Locum SURGICAL REGISTRAR (resident) required 25th November for 1 month and thereafter on week-to-week basis.
Applications to Hospital Secretary. Tel. Bishop's Stortford 963.

**BLACKPOOL VICTORIA HOSPITAL. (354 Beds.)** House OFFICER (orthopædic and traumatic surgery.) Resident pre-registration post recognised for F.R.C.S. available from 1st December, 1957 in the main acute general hospital serving the Blackpool and Fylde area.
Applications, stating age, experience (if any) and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

**BOLTON DISTRICT GENERAL HOSPITAL. (607 Beds.)** RESIDENT HOUSE SURGEON. Vacant 7th December, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.
Applications, stating age, nationality, qualifications, experience and the names of 2 referees, to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton.

**BOURNEMOUTH (near). CHRISTCHURCH HOSPITAL, HAMPSHIRE.** (334 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIANS (Pre-registration Interns) for general medicine required at the above General Hospital.
Applications to the Hospital Secretary immediately.

**BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, WESTBOURNE.** BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER (resident), vacant 20th December, 1957, for E.N.T. duties. The appointment is recognised for the D.L.O. diploma and facilities are provided for studying.
Applications to the Hospital Secretary, Royal Victoria Hospital, Shelley-road, Bournemouth.

**BRISTOL (near). HAM GREEN HOSPITAL, Pill, near BRISTOL.** Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in the Chest Diseases wards of the above Hospital. The Hospital is fully equipped for modern treatment of pulmonary tuberculosis and other diseases of the chest, including regular major thoracic surgery. Opportunity also for work in the Bristol Chest Clinic. Appointment for 1 year, renewable. Post now vacant.
Applications, with testimonials and names of referees, to the Secretary, Ham Green Hospital, Pill, near Bristol.

**BROMSGROVE, WORCESTERSHIRE. HILL TOP HOSPITAL.** (76 Beds.) Regional Thoracic Surgical Centre. Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital. Post vacant January, 1958.
Applications, with the names of 3 referees, to the Hospital Secretary, Bromsgrove General Hospital, Bromsgrove, Worcestershire.

**BROMSGROVE, WORCESTERSHIRE. HILL TOP HOSPITAL.** (76 Beds.) Regional Thoracic Surgical Centre. Applications are invited for the pre-registration post of HOUSE PHYSICIAN at the above Hospital. Post vacant January, 1958.
Applications, with the names of 3 referees, to the Hospital Secretary, Bromsgrove General Hospital, Worcestershire.

**BURTON-ON-TRENT. THE GENERAL HOSPITAL.** HOUSE SURGEON (general, pre-registration) required at the above Hospital immediately. Post recognised for F.R.C.S.
Applications to Group Secretary as soon as possible.

**BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in Anæsthetics, to the above Group of hospitals. The post, which is vacant, is based at Bury General Hospital, and is recognised for the D.A. examination.
Apply, stating full details and names of 2 referees, to H. WILKINSON, Esq., Group Secretary, Bury General Hospital, Walmersley-road, Bury, Lancs.

**CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. ADDENBROOKE'S HOSPITAL, CAMBRIDGE.** CASUALTY OFFICER (Senior House Officer grade) from late-December. Non-resident if desired.
Apply to the Secretary, stating age, nationality, qualifications and experience (with dates) and with copies of three testimonials, by 23rd November, 1957.

**CARDIFF. ROYAL HAMADRYAD GENERAL AND SEAMEN'S HOSPITAL. CARDIFF HOSPITAL MANAGEMENT COMMITTEE.** Resident SENIOR HOUSE OFFICER (medical) required at above Hospital, which caters for acute general medical and surgical cases. Hospital contains acute medical unit, general surgical and genitourinary units and outpatient facilities, also certain amount of casualty work. Consultant staff drawn mostly from United Cardiff Hospitals. Post for 1 year and presents facilities for postgraduate study.
Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

**CHELMSFORD AND ESSEX AND ST. JOHN'S HOSPITALS.** Resident Locum ANÆSTHETIC REGISTRAR required from middle November to 31st December.
Applications to Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford, Essex.

**CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.)** Applications are invited for the post of RESIDENT HOUSE SURGEON. Pre-registration post. The post will become vacant during the middle of November, and offers good surgical experience. Recognised for the F.R.C.S.
Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

**CANTERBURY. KENT AND CANTERBURY HOSPITAL** (277 Beds). GYNÆCOLOGICAL HOUSE SURGEON required at Highland Court annexe, a unit of 25 gynæcological beds situated 3 miles from the above Hospital, with all ancillary services available. Recognised for M.R.C.O.G. 6 months' appointment. Post vacant early in December, 1957. National Health Service salary and conditions.
Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

**CHERTSEY, SURREY. ST. PETER'S HOSPITAL** (late Botley's Park War Hospital). (430 Beds.) ORTHOPÆDIC HOUSE SURGEON (Senior House Officer, or House Officer (intern) grade). 100 orthopædic beds. Post recognised for F.R.C.S. and pre-registration service. Salary in accordance with terms and conditions of National Health Service.
Applications, together with names and addresses of referees, to be sent to the Physician-Superintendent, St. Peter's Hospital, Chertsey, as soon as possible.

**CHERTSEY, SURREY. ST. PETER'S HOSPITAL** (late Botley's Park War Hospital). (430 Beds.) RESIDENT HOUSE SURGEON (intern) required from 17th November, 1957. Salary in accordance with terms and conditions of National Health Service. Recognised for pre-registration service.
Applications, together with names and addresses of referees, to Physician-Superintendent, St. Peter's Hospital, Chertsey, as soon as possible.

**CHESTERFIELD HOSPITAL MANAGEMENT COMMITTEE.** JUNIOR HOSPITAL MEDICAL OFFICER required immediately at Whittington Hall, Chesterfield (356 Beds for Female mentally deficient patients), and Scarsdale Hospital, Chesterfield, where there are 125 Beds for mental patients. Previous experience in psychiatry not essential. Ample opportunities for study. Flat available within the Group.
Apply, with names of 3 referees, to Group Secretary, The Royal Hospital, Chesterfield.

**CHICHESTER. ROYAL WEST SUSSEX HOSPITAL.** (202 acute beds.) RESIDENT HOUSE SURGEON required for 6 months' appointment. National salary scales for either provisionally or fully registered practitioners. Post approved for pre-registration practitioners and F.R.C.S. 8 residents. Vacant 17th November, 1957.
Applications, stating age, experience, qualifications, with references or names of referees, to Senior Administrative Officer.

**CLACTON AND DISTRICT HOSPITAL, Clacton-on-Sea.** (58 Beds.) Applications invited for post of SENIOR HOUSE OFFICER (Resident Surgical Officer). Post tenable for 1 year.
Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

**CREWE AND DISTRICT MEMORIAL HOSPITAL.** (108 Beds acute, and continuation 32 Beds.) 2 pre-registration HOUSE OFFICERS (surgical) required. Approved for F.R.C.S. Vacant January. Salary and conditions in accordance with Whitley Council scale. The appointments may be followed by second post.
Applications, stating age, qualifications, &c., with names of 2 referees, to the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire.

**DARLINGTON MEMORIAL HOSPITAL. Applications** are invited from Male or Female practitioners for the post of SURGICAL AND CASUALTY OFFICER (Senior House Officer) which is recognised for the F.R.C.S. (Eng.). Salary £819 10s. p.a., deduction of £150 p.a. for full residential emoluments. The post is tenable for 12 months, or for a shorter period if desired. The successful candidate will work in conjunction with a Senior Casualty Officer.
Apply, with references, stating age and experience, to the undersigned.
G. W. BECKWITH,
Group Secretary and Secretary Superintendent.

**DERBY. DERBYSHIRE CHILDREN'S HOSPITAL.** HOUSE SURGEON (pre-registration) or SENIOR HOUSE OFFICER required to commence 8th January, 1958. Recognised for D.C.H.
Applications, stating full particulars and names of 2 referees, to be sent as soon as possible to Secretary.

**DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.)** SENIOR HOUSE OFFICER (orthopædic). Vacant 1st January. Recognised for 6 months' "unspecified" training for F.R.C.S.
Apply, giving full details and 2 names for reference, to Secretary.

**DERBY. DERBYSHIRE CHILDREN'S HOSPITAL. (88** Beds.) SENIOR HOUSE OFFICER (pædiatrics) required. Vacant 16th January, 1958. Recognised for D.C.H.
Applications, with 2 names for reference, should be sent as soon as possible to Hospital Secretary.

**DEWSBURY. STAINCLIFFE GENERAL HOSPITAL.** (304 Beds.) Applications are invited for the post of RESIDENT SURGICAL OFFICER (Senior House Officer grade) which falls vacant on 14th January, 1958. The Hospital has a general surgical unit of 52 beds and is recognised for the F.R.C.S.
Applications, with full details, to the Administrative Officer at the hospital.

**DONCASTER ROYAL INFIRMARY. (330 Beds. Recognised** for D.Path.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (pathology) required 16th January. Appointment for 1 year in first instance.
Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th November, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

**DOUGLAS. NOBLE'S ISLE OF MAN HOSPITAL.** (160 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST. Senior House Officer grade. Resident staff of 4. National Health Service salary and conditions of service.
Apply to the Secretary, Noble's Isle of Man Hospital, Douglas.

**DUNDEE. WESTGREEN MENTAL HOSPITAL.** (660 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER required. Teaching school for Queen's College, St. Andrew's University. National salary scale. House available to rent. Some experience in psychiatry and an interest in insulin therapy would be assets.

Applications, stating age, nationality, qualifications and experience, with recent testimonials, to Physician Superintendent.

**EAST ANGLIAN REGIONAL HOSPITAL BOARD.** SURGICAL REGISTRAR, Peterborough Memorial Hospital. Provides wide range of work and experience. 6 months of tenure recognised for F.R.C.S. Appointment for 1 year, renewable for second year.

Applications, stating age, experience, and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 25th November, 1957. Candidates are invited to visit the hospital by direct arrangement with the Hospital Management Committee Secretary at the Hospital.

**EDGWARE GENERAL HOSPITAL, Edgware, Middlesex.** 2 RESIDENT HOUSE PHYSICIANS for above Hospital. Posts vacant 1st December, 1957. 6 months' appointments. Posts recognised for pre-registration purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials to Medical Director of Hospital by 23rd November.

**EDGWARE GENERAL HOSPITAL, Edgware, Middlesex.** RESIDENT HOUSE PHYSICIAN for above Hospital. Post vacant 15th December, 1957. 6 months' appointment. Post recognised for pre-registration purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to three recent testimonials, to Medical Director of Hospital by 29th November, 1957.

**EDGWARE GENERAL HOSPITAL.** (715 Beds.) North West Metropolitan Regional Hospital Board. REGISTRAR (whole time), resident, required in Department of Anæsthesia at above Hospital, which may be visited by direct appointment with Medical Director.

Application forms obtainable from and returnable to Group Secretary, Hendon Group Hospital Management Committee, Edgware General Hospital, Edgware, Middlesex, by 26th November, 1957.

**EDINBURGH. ROYAL INFIRMARY.** Applications are invited from fully registered medical practitioners for the post of RESIDENT HOUSE OFFICER in Obstetrics and Gynæcology, for a period of 1 year from 1st February, 1958. This post is recognised by the Royal College of Obstetricians and Gynæcologists.

Apply by letter, stating age, qualifications and experience, to the Medical Superintendent.

**ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL.** 2 RESIDENT HOUSE PHYSICIANS. Approved pre-registration appointments. Vacant early January, 1958. General medical duties. 6 months appointments.

Applications, with the names and addresses of 2 referees, or copies of 2 recent testimonials, to Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, quoting reference "B" or "S."

**EPPING. ST. MARGARET'S HOSPITAL.** Senior House OFFICER as Casualty Officer and Orthopædic House Surgeon. Duties to commence 3rd December. Recognised training post for F.R.C.S.

Applications, with copies of 2 recent testimonials, to be sent immediately to the Group Secretary, Epping Group Hospital Management Committee, Oak Cottage, The Plain, Epping, Essex.

**EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom,** SURREY. RESIDENT HOUSE SURGEON required 11th December. Pre-registration post recognised for F.R.C.S.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

**GLASGOW. ROYAL HOSPITAL FOR SICK CHILDREN,** YORKHILL, GLASGOW, C.3. Applications are invited for the posts of RESIDENT HOUSE SURGEON (pre-registration) at the above hospital for the term February to August, 1958.

Applications should be addressed to the Medical Superintendent.

**GLASGOW. VICTORIA INFIRMARY.** Senior House OFFICER (anæsthetics). Non-resident post recognised for F.F.A. R.C.S. and D.A.

Applications, with names of 2 referees, to the Secretary, Board of Management for Glasgow Victoria Hospitals, 24, St. Vincent-place, Glasgow, C.1.

**GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL.** SENIOR HOUSE OFFICER in Anæsthetics. The post is approved for D.A. and F.F.A. R.C.S.

Write immediately to Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Govan-road, Glasgow, S.W.1, naming 2 referees.

**GODALMING, SURREY. KING GEORGE V HOSPITAL** FOR DISEASES OF THE CHEST. GODALMING, MILFORD AND LIPHOOK GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (resident). Salary and deduction for board, lodging, &c., in accordance with the national scale (£819 10s.). All modern forms of treatment carried out, including major thoracic surgery, a proportion of the beds being set aside for non-tuberculous chest cases, both medical and surgical. The Hospital is associated with a chest clinic.

Apply, giving names of 3 referees, to the Physician-Superintendent not later than 30th November, 1957.

**HAYWARDS HEATH. HURSTWOOD PARK HOSPITAL.** SENIOR HOUSE OFFICER (neurology), resident, required at the above Hospital. Accommodation for married man. Salary in accordance with the terms and conditions of service with appropriate deduction for residence.

Applications, with the names and addresses of 3 referees, to the Secretary to the Hospital Management Committee, St. Francis Hospital, Haywards Heath, Sussex.

**GUILDFORD. ST. LUKE'S HOSPITAL.** Temporary REGISTRAR or SENIOR HOUSE OFFICER, Group Pathology Laboratory.

Applications, with names of 2 referees, immediately to Hospital Secretary, St. Luke's Hospital, Guildford.

**HALIFAX. ROYAL HALIFAX INFIRMARY.** (301 Beds.) SENIOR HOUSE OFFICER in casualty and orthopædic surgery required. Post recognised for F.R.C.S. and is vacant 1st January, 1958. Salary £819 10s. p.a., with deduction of £150 p.a. for board residence, &c.

Apply to Group Secretary, Royal Halifax Infirmary, Halifax.

**HASTINGS. ROYAL EAST SUSSEX HOSPITAL.** (150 Beds.) Applications are invited for the post of HOUSE SURGEON (pre-registration), vacant on 30th November, 1957. This Hospital is the main surgical hospital in the Hastings area and the post offers excellent experience.

Apply immediately, with 2 testimonials or names of 2 referees, to the Administrator of the Hospital.

**HERTFORD COUNTY HOSPITAL.** (171 Beds. Hospital situated 21 miles from London.) Applications are invited for the appointment of HOUSE SURGEON (general), first or second post. To commence 27th November, 1957. Pre-registration post, recognised under F.R.C.S. regulations.

Applications to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

**HILLINGDON HOSPITAL, Uxbridge, Middlesex.** (621 Beds.) MEDICAL REGISTRAR required on general medical unit. Post recognised for M.D. Lond. (Branch 1). Hospital may be visited by appointment.

Application forms obtainable from and returnable to Group Secretary, Uxbridge Group Hospital Management Committee, The Furze, Pield Heath-road, Hillingdon, Middlesex, by 29th November.

**HITCHIN HOSPITALS, Hitchin, Hertfordshire.** Resident ANÆSTHETIST (Senior House Officer) required 1st January, 1958. Recognised for D.A. and F.F.A.R.C.S. examinations.

Applications, stating age, nationality, qualifications and experience, together with names of 2 referees, to the Medical Administrator, Lister Hospital, Hitchin, by 27th November, 1957.

**HITCHIN. LISTER HOSPITAL.** (305 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR required at above Hospital. Preference given to applicants having experience in medical emergencies. Post vacant 1st January, 1958. Hospital may be visited by direct appointment (Hitchin 3701).

Application forms obtainable from Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton, and returnable by 25th November, 1957.

**HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL.** RESIDENT HOUSE SURGEON required end of November. Recognised as pre-registration post.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to the Medical Administrator, Lister Hospital, Hitchin, as soon as possible.

**HOUNSLOW CHEST CLINIC, 28, Bell-road, Hounslow,** MIDDLESEX. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR (whole time), non-resident, required at above Chest Clinic. Post vacant October. Clinic has associated beds at Ashford Hospital and West Middlesex Hospital. Good general medical experience essential and special experience in diseases of the chest desirable. Candidates may visit Clinic by direct appointment.

Application forms obtainable from and returnable to the Secretary, Staines Group Hospital Management Committee, Ashford Hospital, London-road, Ashford, Middlesex, by 26th November, 1957.

**HOUNSLOW HOSPITAL, Staines-road, Hounslow,** MIDDLESEX. (General acute—81 Beds.) Applications are invited for the appointment of RESIDENT HOUSE PHYSICIAN. Recognised pre-registration appointment for 6 months. Vacant 14th December, 1957.

Applications, stating qualifications and age, together with copies of up to 3 recent testimonials or names for reference, to the Hospital Secretary.

**HUDDERSFIELD ROYAL INFIRMARY.** (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

**HUDDERSFIELD. ST. LUKE'S HOSPITAL.** (235 Beds.) Applications are invited for the post of RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer grade) at the above Hospital, to commence duties on 4th December, 1957. The Group Geriatric Admission Unit is based on this Hospital, which also caters for acute medical and surgical, pædiatric and maternity patients. Salary in accordance with the terms and conditions of service for hospital medical and dental staff, £852 10s.–£55–£1182 10s. p.a. House available for married candidate.

Applications, together with copies of 3 recent testimonials, to be sent to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

**HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE.** HOUSE PHYSICIAN, Pædiatric Unit. Duties at Victoria Children's Hospital for 3 months followed by 3 months on the pædiatric wards, Western General Hospital. An interesting and varied post which includes outpatient and casualty work. This appointment, which commences on 18th December, 1957, is recognised for the D.C.H.

Apply, giving experience, testimonials, &c., to the Secretary, Victoria Hospital for Sick Children, Park-street, Hull.

**HULL. VICTORIA HOSPITAL FOR SICK CHILDREN,** Park-street. Pre-registration or registration post. HOUSE SURGEON required immediately. Recognised for D.C.H. An interesting and varied post which includes outpatient and casualty work.

Applications, together with details of experience, testimonials, &c., to the Hospital Secretary.

**HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the post of SENIOR HOUSE OFFICER in the E.N.T. Department of the Victoria Hospital for Sick Children and the Hull Royal Infirmary. The post, which is vacant on 11th December, is recognised for the F.R.C.S. and D.L.O.

Applications, with testimonials, should be sent to the Hospital Secretary, Victoria Hospital for Sick Children, Park-street, Hull.

**ILKLEY. MIDDLETON HOSPITAL. (430 Beds.)** Resident SENIOR HOUSE OFFICER (medical) required at the above Hospital. This appointment provides for experience in the specialties of tuberculosis and geriatrics.

Applications, stating age, nationality, qualifications, and experience, to Hospital Secretary.

**IPSWICH. FOXHALL HOSPITAL. (102 Beds for chest diseases.)** SENIOR HOUSE OFFICER. The Hospital is actively engaged in the investigation and treatment of all forms of chest disease, including major thoracic surgery and a respiratory function unit. House available.

Applications, with copies of recent testimonials, to Physician-Superintendent, from whom further details may be obtained.

**ISLEWORTH. WEST MIDDLESEX HOSPITAL.** House OFFICER, traumatic and orthopædic surgery unit (58 Beds). Recognised for F.R.C.S. Post vacant 1st December, 1957. Preference given to pre-registration candidates.

Applications to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 26th November.

**KEIGHLEY AND DISTRICT VICTORIA HOSPITAL,** KEIGHLEY, YORKS. (General—139 Beds.) 2 RESIDENT HOUSE SURGEONS (either sex).

General surgery and E.N.T., vacant now.

General surgery and orthopædics, vacant now.

Both recognised for F.R.C.S. and approved pre-registration appointments, tenable for 6 months in first instance. 4 residents on staff.

Applications, with full particulars as to age, nationality, and qualifications, and copies of 2 testimonials, to Group Secretary, St. John's Hospital, Keighley, Yorks.

**KETTERING DISTRICT GENERAL HOSPITAL.** The post of CASUALTY OFFICER (Senior House Officer), recognised for F.R.C.S., is vacant early December, 1957. It offers wide experience of all traumatic conditions, including fractures and some orthopædic cases with charge of 30 Beds.

Applications, accompanied by testimonials, to be sent to the Group Secretary, General Hospital, Rothwell-road, Kettering.

**LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL.** (197 Beds.) HOUSE PHYSICIAN. Vacancy suitable for fully registered or pre-registration applicant. Post vacant.

Applications, with copies of 2 recent testimonials, to be sent to Hospital Secretary.

**LEEDS. UNITED LEEDS HOSPITALS / LEEDS** REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR vacancies.

*General Surgery*

Training will be mainly at the General Infirmary at Leeds, but the person appointed will be required to undertake periodical duties at Regional Hospitals as provided for in the surgical training scheme.

*Obstetrics and Gynæcology* (2 posts)

Appointments will be made jointly to the Teaching and to Regional Hospitals and at least 1 year's training will be give at the Teaching Hospital. The initial year for 1 of the appointments will be at the United Leeds Hospitals and for the other at St. Luke's Hospital, Bradford.

Applications, stating age, qualifications and details of appointments held showing dates, together with the names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 21st November, 1957.

**LEEDS REGIONAL HOSPITAL BOARD.** Registrar vacancies.

*Anæsthetics*

Halifax Group. (Approximately 340 Beds in the surgical specialties.) Resident.

*General Medicine*

Two vacancies in the Hull (A) Group. (294 general medical Beds.) Non-resident.

*Obstetrics and Gynæcology*

York (A) Group. (80 obstetric and 75 gynæcological beds.) Recognised for M.R.C.O.G.

*Ophthalmology*

Huddersfield Group. (23 eye beds and 1500 new outpatients annually.) Non-resident.

*Plastic Surgery*

St. James's Hospital, Leeds. Non-resident. Special plastic and Maxillo-Facial unit. (72 Beds.)

*Psychiatry*

(i) Menston Hospital, near Leeds. (2500 Beds.)

(ii) Oulton Hall Hospital, near Wakefield, and affiliated mental deficiency colonies. (Approximately 400 Beds.) Non-resident.

(iii) Stanley Royd Hospital, Wakefield. (2000 Beds.) Recognised for D.P.M.

(iv) Storthes Hall Hospital, Kirkburton, near Huddersfield. (2750 Beds.)

If desired, facilities for attendance at the Leeds University will be provided, if the successful candidates are studying for the D.P.M.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 27th November, 1957.

**LEEDS REGIONAL HOSPITAL BOARD.** Senior Registrar vacancies.

*Anæsthetics*

Hull A Group of hospitals with additional duties as required in the Hull B and East Riding Groups. Non-resident. Post vacant 1st April, 1958.

*Ophthalmology*

Royal Eye and Ear Hospital, Bradford (34 ophthalmic beds). Additional duties as required in other hospitals in the Bradford A and B Groups. Non-resident.

*Psychiatry*

(i) Storthes Hall Hospital, Kirkburton, near Huddersfield (2600 Beds), and associated clinics. Resident or non-resident.

(ii) De la Pole Hospital, Willerby, Hull (1000 Beds). This Hospital has a high admission-rate and a separate neurosis unit for females. Duties also include visits to the Psychiatric Day Centre, Hull, and an outpatient clinic at Goole. It is anticipated that the successful candidate will undertake 2 clinical sessions (which may include research) in association with the Department of Psychiatry of the University of Leeds. Small flat available for married person, otherwise non-resident.

Candidates for both these appointments should hold the D.P.M. or equivalent qualification.

Applications, stating age, qualifications and details of appointments held showing dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Park-parade, Harrogate, by 21st November, 1957.

**LEICESTER GENERAL INFIRMARY.** Applications are invited for the post of SENIOR HOUSE OFFICER (pathology) now vacant, recognised for the D.Path.

Applications, stating age, qualifications and experience, together with copies of recent testimonials, to the Group Secretary, No. 1 Hospital Management Committee, The Leicester Royal Infirmary, immediately.

**LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS.** ST. PAUL'S EYE HOSPITAL. Applications are invited for a post of Locum REGISTRAR in Ophthalmology to take up duties as soon as possible for the period to 16th February, 1958.

Apply immediately on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

**LLANELLY HOSPITAL, Llanelly. (162 Beds.)** Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in Anæsthetics at the above Hospital. The Hospital is recognised for the D.A. examination. The successful candidate will be granted facilities to attend monthly anæsthetic lectures and discussions which are held at the Cardiff Royal Infirmary.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be sent to the Secretary of the Hospital. T. E. JONES, Group Secretary.

**MAIDSTONE. PRESTON HALL HOSPITAL,** British LEGION VILLAGE, MAIDSTONE, KENT. Applications are invited for the post of SENIOR HOUSE OFFICER at the above Hospital, which contains 330 Beds for the treatment of pulmonary tuberculosis and other chest diseases and includes a major thoracic surgical unit. Married accommodation may become available. Salary £819 10s. p.a., national scale and conditions.

Applications, stating age, qualifications and experience with relevant dates, together with names and addresses of 2 referees, to be sent to the Group Secretary by 6th December, 1957.

**MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT** RADIUM INSTITUTE. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered practitioners for the post of ASSISTANT RESIDENT SURGICAL OFFICER (Senior House Officer grade). The post provides experience in the treatment of tumours and good opportunity for study.

Applications, with full details, including the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

**MANCHESTER REGIONAL HOSPITAL BOARD** invite applications for the post of RESIDENT REGISTRAR in Anæsthetics to the West Manchester Hospital Management Committee with duties primarily at Park Hospital, Davyhulme, but with duties at other hospitals within the group. Post vacant early December.

Application form from Secretary, Park Hospital, Davyhulme.

**MANCHESTER (near). ROYAL MANCHESTER CHILDREN'S HOSPITAL,** PENDLEBURY, NEAR MANCHESTER. SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications invited for the following appointments:—

SENIOR HOUSE OFFICER (resident). Vacant 1st February, 1958. Post tenable for 12 months (6 months medical and 6 months surgical). Candidates should preferably have had previous pædiatric experience.

SENIOR HOUSE OFFICER. Resident surgical post vacant 1st February, 1958. Post tenable for 6 months. Candidates should preferably have had previous pædiatric experience.

SURGICAL HOUSE OFFICER (resident). Vacant 1st February, 1958. Post tenable for 6 months and open to pre-registration graduates.

HOUSE PHYSICIAN, Professorial Unit, University Department of Child Health, resident. House Officer status. Vacant 1st February, 1958. Appointment for period of 6 months and open to pre-registration graduate.

Applications to Hospital Secretary not later than 2nd December, 1957.

**MANCHESTER. WEST MANCHESTER HOSPITAL** MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General hospital—433 Beds.) SENIOR HOUSE OFFICER required for Group Laboratory. Post vacant early December, and tenable for 1 year. Duties which alternate with holder of second similar post include routine general pathology and emergency investigations. Laboratory recognised for D.Path. and D.C.P. examinations. Previous experience not essential.

Application forms from Group Secretary.

**MANCHESTER. UNITED MANCHESTER HOSPITALS.** SAINT MARY'S HOSPITALS, MANCHESTER. Applications are invited for 2 posts of HOUSE OFFICER in Obstetrics, normally but not necessarily for provisionally registered medical practitioners. Salary in accordance with national scale. The appointments are for 6 months from 1st February, 1958.

Application forms may be obtained from the undersigned and returned not later than 25th November, 1957.

A. R. WISE, General Superintendent.

Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

**MANCHESTER. UNITED MANCHESTER HOSPITALS.** SAINT MARY'S HOSPITALS, MANCHESTER. Applications are invited for the post of SENIOR HOUSE OFFICER in Gynæcology. Applicants must have had previous hospital experience in medicine and surgery. The post is recognised for the purpose of the M.R.C.O.G. examination. The appointment is for 6 months starting 1st February, 1958. Salary in accordance with national scale.

Application forms may be obtained from the undersigned and returned not later than 25th November, 1957.

A. R. WISE, General Superintendent.

Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

**MANCHESTER. UNITED MANCHESTER HOSPITALS.** SAINT MARY'S HOSPITALS, MANCHESTER. Applications are invited from registered medical practitioners, Male or Female, for the post of HOUSE PHYSICIAN in the Neonatal Unit of Saint Mary's Hospitals (attached to the University Department of Child Health) for a period of 6 months, vacant on 1st February, 1958. Previous hospital experience essential and pædiatric experience desirable. Duties include the care of the newborn in the maternity department, the care of infants in the infants' ward and work in the clinic under the charge of the Department of Child Health. Salary in accordance with national scale.

Applications, stating qualifications and experience, together with the names of 3 referees, should be sent to the undersigned not later than 25th November, 1957.

A. R. WISE, General Superintendent.

Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

**MANCHESTER. UNITED MANCHESTER HOSPITALS.** MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. SENIOR HOUSE OFFICER (medical) to commence on 19th March, 1958. Whole-time resident post, for 6 months, renewable for a second and possibly a third 6 months. The successful applicant will be attached to the Rheumatism Research Centre but will have some general duties as Deputy Resident Medical Officer.

Application form obtainable from the undersigned, to be returned not later than 30th November, 1957.

G. H. TAYLOR, Secretary.

**MEXBOROUGH. MONTAGU HOSPITAL AND** ANNEXE. (198 Beds—22 obstetrics, 15 gynæcology.) Locum SENIOR HOUSE OFFICER (obstetrics and gynæcology) required 16th to 29th December, 1957. Residential emoluments £150 p.a.

Applications to Secretary, Hospital Management Committee, Fern Bank, Doncaster-road, Rotherham.

**MID-KENT HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the appointment of RESIDENT ANÆSTHETIST for joint duties at the West Kent General Hospital, and the Kent County Ophthalmic and Aural Hospital, Maidstone (total beds 254). The post, which is of Senior House Officer grade, carries a salary of £819 10s. a year less £150 for residential emoluments. Excellent experience under Consultant Anæsthetists is available, and the post is recognised for the F.F.A. R.C.S. examination.

Applications, stating age, nationality, qualifications and experience, together with the names of 2 suitable referees, should be forwarded to the Administrative Officer, West Kent General Hospital, Maidstone.

**MITCHAM. WILSON HOSPITAL, Cranmer-road,** MITCHAM, SURREY. RESIDENT HOUSE PHYSICIAN (not pre-registration). Vacant 25th November.

Applications, stating age, qualifications, &c., with the names and addresses of 2 referees, to the Secretary at above address.

**NANTWICH. BARONY HOSPITAL. Registrar (medical)** required. Vacant January. Salary and conditions in accordance with Whitley Council scale.

Applications, stating age, qualifications, &c., with names of 2 referees, to be sent to the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire within 14 days after publication.

**NANTWICH. BARONY HOSPITAL. Senior House** OFFICER (medical) required. Vacant February. Salary and conditions in accordance with Whitley Council scale.

Applications, stating age, qualifications, &c., with names of 2 referees, to be sent to the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire, within 14 days after publication.

**NEWARK HOSPITAL, London-road, Newark, Notting-**HAMSHIRE. (General.) Resident Locum JUNIOR HOSPITAL MEDICAL OFFICER (medical) required for period 2nd December, 1957–4th January, 1958, inclusive. Salary £19 5s. per week less residential emoluments.

Applications, stating qualifications, with copies of 2 recent testimonials, to the Group Secretary, General Hospital, Nottingham, as soon as possible.

**NEWCASTLE. ST. NICHOLAS HOSPITAL, Gosforth,** NEWCASTLE UPON TYNE, 3. ST. NICHOLAS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (2 years in first instance). This Mental Hospital (1150 Beds) affords opportunities for experience of all modern methods of investigation and treatment. There is an extensive outpatient service, and facilities are given to study for the D.P.M.

Applications, giving details of qualifications and experience, together with names and addresses of 2 referees, to be submitted to the Group Secretary.

**NEWCASTLE GENERAL HOSPITAL. (838 Beds.) Senior** HOUSE OFFICER for Orthopæd'c Department. Vacant 1st January, 1958.

Applications, together with names and addresses of 2 referees, should be sent to the Secretary, Newcastle General Hospital, Newcastle upon Tyne, 4.

**NEWCASTLE REGIONAL HOSPITAL BOARD. Resident** REGISTRAR in Anæsthetics for duties at hospitals in the Sunderland area (1947 Beds). Post offers practical experience under supervision of visiting anæsthetists, and is recognised for F.F.A. R.C.S., and D.A. Opportunity will be given to attend Newcastle Medical School for lectures.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

**NEWCASTLE UPON TYNE HOSPITAL MANAGE-**MENT COMMITTEE. DEPARTMENT OF NEUROLOGICAL SURGERY, REGIONAL UNIT. The post of SENIOR HOUSE OFFICER, either resident or non-resident, is now vacant.

Applications, together with names and addresses of 2 referees, should be sent to the Secretary, Newcastle General Hospital, Newcastle upon Tyne, 4.

**NEWMARKET GENERAL HOSPITAL, Suffolk. Applica-**tions are invited for the post of HOUSE PHYSICIAN, vacant 21st December, 1957. Duties include house charge of general medical and pulmonary tuberculosis beds. The post is recognised for pre-registration, is resident and tenable for 6 months. Salary in accordance with national scale.

Applications, with 3 recent testimonials, to Medical Superintendent.

**NORTHAMPTON GENERAL HOSPITAL. (500 Beds.)** Vacancy 1st February, 1958, for SENIOR HOUSE OFFICER, E.N.T. Department. Recognised for F.R.C.S. and for D.L.O. Appointment to 30th September, 1958, in first instance.

Applications as soon as possible to S. G. HILL, Superintendent.

**NORTHAMPTON (near). CREATON HOSPITAL. (138** Beds.) Applications are invited from suitably qualified medical practitioners for the post of SENIOR HOUSE OFFICER. The Hospital has 138 Beds, and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a major thoracic surgical unit for tuberculous and non-tuberculous diseases of the chest.

Applications, stating age, experience and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton, within 7 days of the appearance of this advertisement.

**NORTHAMPTON. ST. ANDREW'S HOSPITAL. Appli-**cations are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER. The successful candidate will work in the hospital and outpatient clinics. The hospital is recognised for training for the D.P.M. Exceptional postgraduate facilities are available. Salary £669 10s. p.a., together with full residential emoluments, valued for superannuation purposes at £150 p.a. If married, unfurnished house will be provided with light, coal, laundry, and garden produce. The hospital operates outside the National Health Service, but reciprocity has been granted between the National Health Service superannuation scheme and the Hospital superannuation scheme, so that years of service are transferable in either direction.

Applications, stating age, qualifications, experience, &c., together with copies of 3 recent testimonials, to be addressed to the Medical Superintendent.

**NORTHAMPTON. ST. CRISPIN HOSPITAL, Duston,** NORTHAMPTON. (1120 Beds.) SENIOR HOUSE OFFICER required. Salary according to national scale (£745 p.a.). Accommodation is available at the Hospital. The Hospital is approved for training for the D.P.M. of the Conjoint Board and the post offers excellent opportunities for participation in inpatient and outpatient work, E.E.G. investigations, and child psychiatry. There is a modern Admission Unit and an annual admission-rate of over 850 patients p.a. Regular case conferences are held.

Applications, giving full details and names of 3 referees, to be sent to the Physician-Superintendent at the Hospital within 14 days.

**NOTTINGHAM. HIGHBURY HOSPITAL, Bulwell,** NOTTINGHAM. SENIOR HOUSE OFFICER (surgical) required at the above Hospital. Good opportunity for obtaining experience in all types of general surgery. Vacancy with effect, 1st December, 1957.

Applications, stating age, qualifications, experience and nationality, together with copies of testimonials, to be sent to Hospital Secretary.

**OTLEY, YORKSHIRE. THE GENERAL HOSPITAL.** (172 Beds.) SENIOR HOUSE SURGEON (Senior House Officer grade) in General and Orthopædic Surgery (with secondary duties to other specialties) required to work under full consultant staff who are members of the teaching staff of Leeds University. Post recognised under F.R.C.S. regulations.

Applications, stating age, nationality, and experience, with names of 2 referees, to Group Secretary, The General Hospital, Otley.

**POOLE GENERAL HOSPITAL, Poole. (310 Beds.)** BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (pre-registration) required for post vacant 22nd November, 1957.

Applications to Hospital Secretary.

**OXFORD. UNITED OXFORD HOSPITALS. Applica-**tions invited for post of non-resident REGISTRAR in the Department of Pathology, Radcliffe Infirmary, to commence as soon as possible. There will be opportunities for working in all the departments including neuropathology.

Applications on forms obtainable from the Administrator, Radcliffe Infirmary, Oxford, should be received not later than 30th November.

**OXFORD. UNITED OXFORD HOSPITALS.** Applications are invited for posts of HOUSE OFFICER and SENIOR HOUSE OFFICER in Accident Service, Radcliffe Infirmary, with effect from 1st January and 1st February, 1958, respectively, for a period of 6 months.

Applications, stating age, qualifications and experience, together with the names for reference purposes, should be received by the Administrator, Radcliffe Infirmary, Oxford, by 30th November.

**PERTH. COUNTY AND CITY OF PERTH GENERAL HOSPITALS.** The following House Officer posts will fall vacant on 1st February, 1958:—

**Bridge of Earn Hospital**

*1 SENIOR HOUSE SURGEON (Fracture and Orthopædic Unit).
*3 HOUSE SURGEONS (Fracture and Orthopædic Unit).
*3 HOUSE SURGEONS (general surgical wards).
†1 HOUSE SURGEON or SENIOR HOUSE SURGEON (E.N.T. ward).
3 HOUSE PHYSICIANS (general medical wards).
‡1 HOUSE OFFICER (gynæcology and obstetrics).

**Perth Royal Infirmary**

*2 HOUSE SURGEONS (general surgical wards).
*1 HOUSE SURGEON or SENIOR HOUSE SURGEON (casualty).
3 HOUSE PHYSICIANS (general medical wards).

*Notes:*

1. Senior House Officer posts are tenable for 12 months and Junior House Officer posts for 6 months, with the exception of the gynæcology and obstetrics post shown under Bridge of Earn Hospital: this post is tenable for 12 months and consists of 6 months gynæcology at Bridge of Earn Hospital, followed by 6 months obstetrics at Perth Royal Infirmary.
2. All Junior House Officer posts are recognised for pre-registration hospital service.
3. Posts marked * are recognised by the Royal College of Surgeons under the regulations for the F.R.C.S.
4. Post marked ‡ is recognised both for gynæcology and obstetrics under the regulations for the M.R.C.O.G. The obstetrics post at Perth Royal Infirmary is also recognised for the Diploma in Obstetrics of the Royal College of Gynæcologists.
5. Post marked † is recognised under the regulations for the D.L.O.

Applications, giving age, qualifications, experience, and names of 2 referees, should be sent to the Group Medical Superintendent, Perth Royal Infirmary, Perth.

**PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL.** Vacancies exist in the following departments:—

HOUSE SURGEON (pre-registration post), vacant 1st December. Recognised for the F.R.C.S. Devonport Hospital.

HOUSE SURGEONS (pre-registration posts), vacancies 9th December, 1957, 1st and 4th January, 1958. Recognised for the F.R.C.S. Greenbank Road Hospital.

In both cases send names of 3 referees to the Group Secretary, 7, Nelson-gardens, Devonport.

**PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. FREEDOM FIELDS HOSPITAL.** Central Casualty Department.

SENIOR HOUSE OFFICER in Casualty, vacant 1st January, 1958. Recognised for the F.R.C.S.

Applications, stating names of 3 referees, to be sent to the Group Secretary.

**PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.** Applications are invited for the appointment, vacant on 1st January, 1958, of REGISTRAR in the Chest Services of the Group for duties at the Portsmouth Chest Clinic and tuberculosis and non-tuberculosis beds at the Infectious Diseases Hospital and Saint Mary's Hospital, Portsmouth, including experience with a major thoracic surgery unit.

Forms of application may be obtained from the Group Secretary, Saint Mary's Hospital, Milton, Portsmouth, which should be returned to him, duly completed, on or before 25th November, 1957. Candidates may visit the above Clinic and Hospital by arrangement with the Group Secretary.

**PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.**

**Royal Portsmouth Hospital**

(1) **Orthopædic Department** (104 Beds)
(a) SENIOR HOUSE OFFICER required. Vacant 1st December, 1957.
(b) HOUSE OFFICER (pre-registration), vacant now.
(2) SENIOR HOUSE SURGEON (70 surgical beds). Vacant now.

**Queen Alexandra Hospital** (78 medical beds.)

HOUSE PHYSICIAN (pre-registration). Vacant 1st January, 1958.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

**READING. BATTLE HOSPITAL. (391 Beds.)** Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON in the Accident and Orthopædic Department. Post vacant now. F.R.C.S. recognised. Also casualty duties.

Apply, stating age, qualifications with dates, nationality, present post, with 1 copy of recent testimonial, to Hospital Secretary.

**READING. ROYAL BERKSHIRE HOSPITAL. (398 Beds.)** Applications are invited from registered and provisionally registered medical practitioners, Male and Female, for resident post of HOUSE SURGEON, vacant 1st December, 1957, and tenable for 6 months.

Write, before 15th November, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary.

**READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the appointment of SENIOR HOUSE OFFICER to the Department of Geriatric Medicine which is being developed at Battle Hospital, Reading, under the charge of a Consultant Geriatric Physician.

Further particulars may be obtained from the Group Secretary, 3, Craven-road, Reading, to whom applications, stating age, qualifications and names of 3 referees, should be addressed.

**READING AREA DEPARTMENT OF MEDICINE.** Applications are invited from registered and provisionally registered medical practitioners for 2 posts as RESIDENT HOUSE PHYSICIAN vacant 1st December, 1957, for a period of 6 months. Successful candidates will be required to carry out duties at the following Reading hospitals: Royal Berkshire (398 Beds), Battle (390 Beds), and Prospect Park (104 Beds).

Write immediately, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

**ROCHESTER, KENT. ST. BARTHOLOMEW'S HOSPITAL. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the post of CASUALTY OFFICER (Senior House Officer grade) (1 of 2 in the department) which offers excellent experience with fractures and emergency surgery, and presents facilities for studying. Recognised for F.R.C.S. Post vacant now and tenable for 1 year. Salary £819 10s. p.a.

Applications, stating age, nationality, qualifications and experience, with recent testimonials, to be sent to the Hospital Secretary.

**ROCHFORD, ESSEX. GENERAL HOSPITAL. (620 Beds.)** Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER to work in the Chest Unit (72 Beds) at the General Hospital, Rochford, and at the Lancaster House Chest Clinic, Southend-on-Sea, to commence duty mid-December. Good experience in general medicine essential, and previous experience in tuberculosis and diseases of the chest desirable. Salary £819 10s. p.a.

Applications, stating age, &c., to be sent to the undersigned by 23rd November, 1957. J. C. FIELD, Secretary.

**ROCHFORD, ESSEX. GENERAL HOSPITAL. (620 Beds.)** HOUSE PHYSICIAN (pre-registration) required. Vacant 1st December, 1957.

Applications, &c. (1 testimonial only necessary from pre-registration applicant seeking first appointment) to be sent to the undersigned by 19th November, 1957.

J. C. FIELD, Secretary.

**ROCHFORD, ESSEX. GENERAL HOSPITAL. (620 Beds.)** Applications are required from pre-registration candidates for a 6 months' appointment of HOUSE SURGEON (recognised for F.R.C.S.) at the above Hospital. Post vacant 24th November, 1957.

Applications, &c. (1 testimonial only necessary from pre-registration candidates seeking first appointment) to be sent to the undersigned by 19th November, 1957.

J. C. FIELD, Secretary.

**ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.)** ORTHOPÆDIC HOUSE SURGEON (resident) required in the Orthopædic and Accident Unit from 3rd December, 1957. The service consists of 100 Beds equally divided between traumatic surgery and "cold" orthopædics. Post is recognised for pre-registration purposes and for F.R.C.S.

Applications to be sent to Group Secretary, Romford Hospital Management Committee, Oldchurch Hospital, as soon as possible.

**ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.)** RESIDENT PÆDIATRIC HOUSE PHYSICIAN (Male or Female) required from 4th December, 1957. The Department includes a Premature Baby Unit of 9 Cots and 50 children's medical beds.

Applications should be forwarded immediately to the Secretary, Romford Group Hospital Management Committee, at the Hospital.

**ROMFORD, ESSEX. RUSH GREEN HOSPITAL. (301 Beds.)** GYNÆCOLOGICAL HOUSE SURGEON, Male or Female, required from 1st January, 1958. Unit comprises 35 gynæcological and 6 maternity beds. Resident post open to either pre-registration applicants or to fully registered practitioners.

Applications to Medical Superintendent as soon as possible. Hospital may be seen by arrangement. Tel. Romford 46066.

**SALISBURY GENERAL HOSPITAL.** Applications are invited for the appointment of RESIDENT OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEON (recognised by R.C.O.G.)/HOUSE SURGEON from 1st December, 1957, for a period of 6 months in each post commencing with House Surgeon post.

The posts are open to pre-registration candidates.

Apply, giving names and addresses of 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

**ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire.** (384 Beds.) HOUSE SURGEON (House Officer grade) required for 1 of the 2 surgical teams from 19th December, 1957. Post recognised for F.R.C.S. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

**SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD.** Applications are invited for the following appointments, which will be for 1 year in the first instance:—

SENIOR REGISTRAR in Radiodiagnosis, based at the Royal Infirmary, Glasgow.

REGISTRAR in Anæsthetics, based at Stobhill General Hospital, Glasgow.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 30th November, 1957.

**SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD** invite applications for 2 Posts under the Combined Training Scheme in Hospital and General Practice in which the Board and the Executive Council for the County of Inverness are associated. The scheme provides a training of 2 years' duration for young medical practitioners intending to enter general medical practice or a specialty. Concurrent experience is given in various departments of the hospitals and with selected general practitioners in the town of Inverness. The trainees' time is divided equally between hospital work and general practice. The posts are non-resident. They are graded at Senior House Officer or Registrar level according to the hospital duties and the corresponding salaries are £819 10s. rising in the second year to £850, and £850 rising in the second year to £935.

Candidates should apply by 30th November, 1957, on forms obtainable from the undersigned, by whom further particulars will be supplied on request.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

**SHEFFIELD. CITY GENERAL HOSPITAL. (858 Beds.** Recognised for F.R.C.S. examination.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT CASUALTY REGISTRAR required 23rd November. The successful candidate to reside at the Hospital when on duty (including "on call" duty). Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th November, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

**SHEFFIELD. UNITED SHEFFIELD HOSPITALS** BOARD OF GOVERNORS AND SHEFFIELD REGIONAL HOSPITAL BOARD. Reciprocal training scheme for Senior Registrars. 3 Whole-time SENIOR REGISTRARS in Radiology required with initial tenures of appointment respectively as follows:—

(1) United Sheffield Hospitals.
(2) City General Hospital, Sheffield and Barnsley or Rotherham Group of Hospitals.
(3) Leicester Royal Infirmary.

Candidates should hold a Diploma in Diagnostic Radiology. Appointments for 1 year in first instance and renewable thereafter annually. The successful candidates will be transferred as appropriate to a regional hospital or the teaching hospitals, for the second phase of the appointment in accordance with the arrangements under the Reciprocal training scheme. Renewal of appointment and transfer will be subject to satisfactory work and progress.

Further details and form of application from the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 2nd December, 1957.

**SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL.** (500 Beds.) Senior House Officer to work as CLINICAL PATHOLOGIST to Group Laboratory. Appointment tenable for 1 year, resident or non-resident. Vacant 1st January, 1958. A Unit of the Public Health Laboratory service is housed in the same building and there are facilities for training in all the 4 main branches of pathology.

Applications to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury, naming 3 referees.

**SHREWSBURY. ROYAL SALOP INFIRMARY. (241** Beds.) SENIOR HOUSE OFFICER (casualty), resident or non-resident. Duties from 9 A.M. to 6 P.M. daily, except Saturday which will be 9 A.M. to 1 P.M. Applicant required to do 1 weekend's duty in 3. Post recognised for F.R.C.S. Vacant 14th December, 1957.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

**SOUTHAMPTON GENERAL HOSPITAL. (474 Beds.)** RESIDENT HOUSE PHYSICIAN required mid-November. Pre-registration candidates eligible.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

**SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL.** (274 Beds.) RESIDENT HOUSE SURGEON required. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

**SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL.** (274 Beds. Recognised for F.R.C.S.) ORTHOPÆDIC HOUSE SURGEON (post recognised for pre-registration service and tenable for 6 months). The Hospital is the centre to which all trauma from a large industrial town and port is directed, thus providing excellent experience in the treatment of traumatic conditions; patients with orthopædic conditions are drawn from a wide area.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

**SOUTHEND-ON-SEA GENERAL HOSPITAL.** Applications are invited for appointment as HOUSE PHYSICIAN (pre-registration). Post vacant 16th December, 1957.

Applications, stating age, qualifications and previous experience, with copies of recent testimonials (1 testimonial sufficient from applicants for first appointment) to reach the undersigned by 26th November, 1957. J. C. FIELD, Secretary.

**SOUTHEND-ON-SEA GENERAL HOSPITAL.** Applications are invited from registered or provisionally registered practitioners for appointment as RESIDENT HOUSE SURGEON. Post vacant 6th December, 1957.

Applications, stating age, qualifications and previous experience, with copies of recent testimonials (1 testimonial sufficient from applicants for first appointment), should reach the undersigned by 21st November, 1957. J. C. FIELD, Secretary.

**SOUTHEND-ON-SEA GENERAL HOSPITAL.** Applications are invited for appointment as SENIOR HOUSE OFFICER to the Orthopædic and Fracture Department. Post vacant 8th December, 1957. The Orthopædic and Fracture Department is the centre for reference of all cases from a large surrounding area, and the post offers excellent experience in all aspects of orthopædic and traumatic surgery under the supervision of and with instructions from the Consultant in charge. Post recognised for the F.R.C.S. Resident or non-resident.

Applications, stating age, qualifications and experience, together with copies of recent testimonials, should be sent to the undersigned by 20th November, 1957. J. C. FIELD, Secretary.

**SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL.** SENIOR HOUSE OFFICER (Casualty) required, working with Casualty Registrar in busy Casualty Department. Post recognised for F.R.C.S. Experience given in plastic and orthopædic cases.

Applications, with names of 2 referees, to Secretary.

**STRATFORD-ON-AVON HOSPITAL. (163 Beds.)** RESIDENT HOUSE SURGEON. New post providing excellent experience.

Applications, with 2 recent testimonials, to Hospital Secretary.

**STOKE-ON-TRENT. ORTHOPÆDIC HOSPITAL,** HARTSHILL, STOKE-ON-TRENT. (78 Beds.) SENIOR HOUSE OFFICER (orthopædics) required. Duties also at North Staffordshire Royal Infirmary.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

**STOKE-ON-TRENT. CITY GENERAL HOSPITAL.** (815 Beds.) HOUSE OFFICER (general surgery) required, vacant now. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

**SWANSEA HOSPITAL, Swansea. (413 Beds.) Glantawe** HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of CASUALTY OFFICER of Junior Hospital Medical Officer grade, at the above Hospital. Resident or non-resident. Vacancy 5th December, 1957.

Full particulars, stating age, qualifications and experience, together with the names of 2 referees, should be forwarded to the Secretary of the Hospital.

T. E. JONES, Group Secretary.

**TAUNTON AND SOMERSET HOSPITAL, Taunton,** SOMERSET. (423 Beds.) HOUSE OFFICER (general surgery) required. Pre-registration post recognised for F.R.C.S. 2 posts vacant, 28th November, 1957, and 9th January, 1958, respectively.

Applications, stating age, nationality and qualifications, to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton, Somerset, immediately.

**TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the appointment of SENIOR HOUSE OFFICER (anæsthetics) for duties at hospitals within this Group. Resident or non-resident. The post is vacant on 1st December and is recognised for the D.A. and F.F.A. R.C.S. Some previous experience desirable but not essential. Full establishment of junior medical staff.

Applications, with copies of 3 references, to be addressed to the Group Secretary, Worsley House, North Ormesby Hospital, Middlesbrough.

**TORQUAY. TORBAY HOSPITAL. (166 general beds.)** RESIDENT HOUSE OFFICER (surgical), Male or Female, required approximately 15th December, 1957. Post recognised for F.R.C.S. and pre-registration purposes. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality and age, together with copy testimonials (quoting reference F.955/84), to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

**TORQUAY. TORBAY HOSPITAL. (166 acute general** beds.) HOUSE OFFICER (medicine), Male or Female, required early January 1958. Pre-registration appointment. General duties which will include some work in the E.N.T., the Ophthalmic and Radiotherapy Departments.

Applications, stating qualifications, nationality, age, together with copy testimonials (quoting ref. F.955/85) to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

**TORQUAY. TORBAY HOSPITAL. Resident Casualty** OFFICER (Senior House Officer status) required approximately 23rd December, 1957. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality, age (quoting Ref. F.955/86), with copy testimonials, to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

**WARRINGTON INFIRMARY. Applications are invited** from Males and Females for the post of RESIDENT CASUALTY OFFICER (graded as Junior Hospital Medical Officer) at the above Hospital. The post is now vacant and is recognised for the F.R.C.S. Scale of salary £852 10s.–£955–£1182 10s., less a deduction of £170 for the residential emoluments. A whole-time Senior Hospital Medical Officer is in charge of the Department.

Applications, stating age, experience and qualifications, should be forwarded to—

HENRY L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

**WATFORD. SHRODELLS HOSPITAL. (320 Beds.)** Applications are invited for the post of HOUSE PHYSICIAN (pre- or post-registration), to take up duty about 1st December.

Applications, with copies of 2 recent testimonials, should reach the Medical Officer in Charge as soon as possible.

**WARWICK (near). KING EDWARD VII MEMORIAL** CHEST HOSPITAL, Hertford Hill, near WARWICK. (228 Beds.) SENIOR HOUSE OFFICER (resident). Applications invited for this appointment in modern Thoracic Surgical Unit. All forms of major and minor thoracic surgery undertaken. Post offers wide general training in cardiac, œsophageal and pulmonary surgery. Facilities available for postgraduate study. Previous experience in specialty not essential.

Applications to Medical Superintendent.

**WIGAN. ROYAL ALBERT EDWARD INFIRMARY.** SURGICAL REGISTRAR (resident) required at above Infirmary. Preference given to holders of higher surgical qualifications. Post recognised for F.R.C.S.

Apply, with names of 2 referees, to Secretary, Wigan and Leigh Hospital Management Committee, Knowsley House, Wigan.

**WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL.** (315 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant 1st December.

Applications, with copies of 2 testimonials, to the Group Secretary.

**WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL.** (315 Beds.) SENIOR HOUSE OFFICER (orthopædics) required. Post recognised F.R.C.S. Wide experience available under Area Orthopædic team. Appointment for 6 months in first instance. Vacant immediately.

Applications, with copies of 2 testimonials, to the Group Secretary.

**WINDSOR. KING EDWARD VII HOSPITAL. House** SURGEON in General and Orthopædic Surgery required, Male or Female, for post vacant 11th December. Pre-registration post—Hospital recognised for F.R.C.S.

Applications, stating age, qualifications, with dates, and nationality, to Secretary.

**WINDSOR. KING EDWARD VII HOSPITAL. House** SURGEON in General Surgery required, Male or Female, for post vacant 28th December. Pre-registration post, recognised for F.R.C.S.

Applications, stating age, nationality, qualifications with dates, and copies of recent testimonials, to Secretary by 27th November.

**WOLVERHAMPTON. NEW CROSS HOSPITAL. (634** Beds.) SENIOR HOUSE OFFICER or HOUSE OFFICER (pre-registration) in Medicine. Acute medical beds. Vacant now.

Applications to Hospital Secretary.

**WOLVERHAMPTON. NEW CROSS HOSPITAL. (634** Beds.) Pre-registration HOUSE OFFICER in General Surgery. Vacant now.

Applications to the Hospital Secretary.

**UGANDA MEDICAL DEPARTMENT. Hospital Appoint**ments. Applications are invited for:—

(*a*) Male RESIDENT MEDICAL OFFICERS (interns) at Mulago Hospital, Kampala, Uganda, for normal internship duties in the Departments of Medicine, Surgery and Obstetrics. Applicants must have fulfilled their National Service obligations. Appointments on agreement for a period of 12 months with salary rate £618 a year for first 6 months and £645 a year for second 6 months and a messing allowance of £144 a year. Free furnished quarters, including linen, cutlery, china and glass, together with light, fuel and water, provided. Married quarters not provided; married candidates may *not* be accompanied by their wives. Free air passage provided on appointment and on satisfactory completion of agreement. Selected candidates may apply for appointments to the Medical Branch of Her Majesty's Overseas Civil Service on the expiration of internships. Candidates should verify from their licensing bodies that the posts at the Mulago Hospital are approved by them for pre-registration training under the Medical Act, 1950.

(*b*) RESIDENT MEDICAL OFFICER (for doctor already on the British Medical Register) at the European and Asian Hospital Kampala, to work under the direction of a Specialist Surgeon, Physician or Obstetrician. The general administration of the hospital (which has 92 Beds) is under a Medical Superintendent. Appointment will be on contract for 1 year with gratuity (taxable) of 13½% salary and then selected officers may be offered appointment to permanent and pensionable post on 2 years probation. Candidates from National Health Service may retain superannuation rights and receive gratuity (taxable) of 20% of salary after engagement. Salary scale ranges from £1284 to £2115 a year. Starting salary determined according to qualifications and experience. Free passages (up to 4 tourist-class air fares) provided in both directions for officer, wife, and dependent children. Quarters are provided at rental between £21 and £78 a year; items of hard furniture supplied at rental of £12 to £24 a year. Income-tax at local rates.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting reference BCD. 117/9/016).

**U.S.A. BETHESDA HOSPITAL, Cincinnati 6, Ohio, U.S.A.** INTERNS—Rotation through Obstetrics, Medicine, Pediatrics and Surgery in a 12-month broad teaching programme. We desire applications from graduate medical doctors giving full details in first letter. $210 per month stipend; access to inexpensive meals; furnished room; uniforms; laundry; hospitalisation, and will advance passage one way.

Please apply to the Superintendent.

**CANADA. REGINA GENERAL HOSPITAL, Regina,** SASKATCHEWAN, CANADA. Vacancies exist for appointments as RESIDENT and ASSISTANT RESIDENT in services of radiology, pædiatrics and obstetric/gynæcologist in 800-Bed General Hospital. All services very active. Stipend $200 per month for Assistant Resident: $250 for Residents. Full maintenance provided.

Apply: Superintendent.

**CANADA. OSHAWA GENERAL HOSPITAL, Alma-**street, OSHAWA, ONTARIO. (Modern 350-Bed General Hospital.) Has a vacancy on INTERN STAFF. Training programme in effect. Applicants will be considered for immediate acceptance and also for future appointments. Uniform, room, meals, laundry supplied, in addition to $100 per month.

Reply to W. A. HOLLAND, Superintendent.

**MICHIGAN, U.S.A. OAKWOOD HOSPITAL, Dearborn,** MICHIGAN. Applications are invited for 1 or 2-year approved GENERAL PRACTICE RESIDENCY in modern 234-Bed General Hospital 10 miles from Detroit. Excellent facilities. Hospital approved for exchange-visitor programme. Beginning monthly salary $250 if single, $300 if married. Free housing.

Apply: Director.

**BRITISH GUIANA. CATHOLIC HOSPITAL, George-**TOWN, BRITISH GUIANA.

RESIDENT SURGEON required immediately. Commencing salary £1800/£2000 dependent on experience, with quarters or house allowance and contributing pension scheme. Initial contract for 3 years.

Apply, stating qualifications, experience in general surgery, with references, to the undernamed.

RESIDENT MEDICAL OFFICER also required immediately. Commencing salary £1100/£1200 dependent on experience, with quarters, and contributory pension scheme. Initial contract 3 years.

Apply, with references, as below:

H. R. GUY, 23, Lawrence-lane, London, E.C.2.

## Public Appointments

**BRIDLINGTON. BOROUGH OF BRIDLINGTON,** URBAN DISTRICT OF FILEY, URBAN DISTRICT OF DRIFFIELD, RURAL DISTRICT OF DRIFFIELD, EAST RIDING COUNTY COUNCIL. Combined appointment of DISTRICT MEDICAL OFFICER OF HEALTH AND COUNTY DIVISIONAL MEDICAL OFFICER. Applications are invited from duly qualified medical practitioners possessing a Diploma in Public Health or similar qualification for the combined appointment of Medical Officer of Health for the Borough of Bridlington, the Filey and Driffield Urban Districts and the Driffield Rural District, and County Divisional Medical Officer for the County Council within the same area together with the Bridlington Rural District (total population 56,700). The successful candidate will be required to take up duty on or about 1st April, 1958. The offices will be held as a joint whole-time appointment. The total combined salary will be £1881 13s. 4d., rising by annual increments to £2208 6s. 8d. Conditions of service in accordance with the Whitley Council recommendations (Medical Council Committee 'C'). The officer will be required to provide a motorcar for the purpose of carrying out his duties and will be paid travelling allowances in respect thereof. The appointment, which will be superannuable, will be subject to the provisions of Section 110 of the Local Government Act, 1933, and the Sanitary Officers (Outside London) Regulations, 1935 and 1951.

Forms of application (and further details regarding the appointment) may be obtained from the Clerk of the County Council, County Hall, Beverley, to whom such forms should be returned by not later than Monday, 25th November, 1957.

**YORKSHIRE. COUNTY COUNCIL OF THE WEST** RIDING OF YORKSHIRE. Appointment of ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER. Applications are invited from registered medical practitioners, men or women, for posts in the following areas:—

Division No. 17. Spenborough M.B. and Mirfield Urban District.

Division No. 20. Kirkburton, Denby Dale, Colne Valley, Meltham, Holmfirth, and Saddleworth Urban Districts.

The Assistant will be on the staff of the County Medical Officer's Department but will work under the administrative direction of the Divisional Medical Officer for the area. The duties will be mainly clinical in the School Health and Infant Welfare Services, but other county health duties may be included by the Divisional Medical Officer. The scale of salary is £1050–£1475 p.a. A minimum of 3 years' experience since qualification is desirable and the possession of a Diploma in Child Health will be an advantage. Travelling and subsistence allowances according to the County Council's scale are payable in addition to salary. The posts are superannuable and successful applicants will be required to pass a medical examination as to physical fitness.

Forms of application can be obtained from the undersigned, to whom they should be returned not later than 30th November, 1957.

J. WOOD-WILSON,
County Hall, Wakefield. County Medical Officer.

**GOVERNMENT OF HONG KONG. Male Government** PATHOLOGIST required for duties including vaccine production, public health laboratory work, clinical pathology and post-mortem work. The post is a senior one and candidates (who should be under 45 years of age) should possess qualifications registrable in the United Kingdom, and have had 5 years experience in pathology including bacteriology; postgraduate degree or diploma in pathology or bacteriology desirable. Appointment on contract for 3 years.

Emoluments:—

(*a*) Salary £2325 a year.

(*b*) Expatriation Pay £237 10s. a year.

(*c*) Temporary variable cost-of-living allowance (present rates):—

| | |
|---|---|
| Single Officers .. .. .. .. .. | £127 a year |
| Married Officers without children .. | £413 a year |
| Married Officers with children .. | £696 a year |

(*d*) Gratuity (taxable) £250 a year.

Free passages for officer, wife, sons under 18 and daughters under 21, up to 5 passages in all. Quarters when available at rental not exceeding 1/7th of basic salary.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD. 117/51/025).

**MANCHESTER. CITY OF MANCHESTER HEALTH** DEPARTMENT. MEDICAL OFFICER (Maternity and Child Welfare). Applications are invited from registered medical practitioners (Male or Female) for the above position on the permanent staff. Applicants should have obstetric and paediatric experience and will be required to undertake duties principally in Maternity and Child Welfare Clinics. Possession of the D.Obst. R.C.O.G., D.P.H. or D.C.H. qualifications will be an advantage. Salary scale £1050 rising to £1475 p.a. The appointment is subject to a medical examination and the City Council's conditions of service.

Application forms obtained on request, must be returned to the Town Clerk, Town Hall, Manchester, 2, and not to any member of the Council, by 23rd November, 1957. Envelopes must be endorsed "Medical Officer, Nursing Services Division." Canvassing is prohibited.

**NAVY, ARMY AND AIR FORCE INSTITUTES.** Applications are invited from general practitioners in the undernoted towns for the appointment in a part-time capacity as MEDICAL OFFICERS to this Corporation. Successful applicants would be required to examine and report on the condition of employees of the Corporation who may be referred to them from time to time. Fees for this work will be paid on a scale agreed with the British Medical Association.

Applications, giving details of qualifications and experience, should be sent to the Chief Medical Officer, Navy, Army and Air Force Institutes, Kennington-lane, London, S.E.11, not later than 30th November, 1957.

The towns for which applications are invited are:—

AYR STIRLING ROSYTH LANARK PERTH

**THE PUBLIC SERVICE OF PAPUA AND NEW GUINEA**

VACANCY

**Director of Public Health**

Salary *£A3250 (unmarried), £A3375 (married).

*Rates quoted include territorial allowance of £A200 (unmarried) and £A325 (married). Additional territorial allowance is paid under following conditions:—

After 5 years' service but less than 7 £A25

After 7 years' service £A50.

***Qualifications.*** Recognised Medical Degree with Diploma Public Health or Tropical Medicine and Hygiene; proven administrative ability of high order including wide experience medical administration under tropical conditions.

***Duties.*** Responsible for efficient functioning of Department of Public Health.

***Eligibility.*** Male British subjects.

***Appointment.*** Permanent or period appointment according to age.

***Location.*** Headquarters at Port Moresby.

***Leave.*** 3 months after each 21 months in territory. Additional 3 months' leave after each 6 years' service and 6 months' furlough after 20 years' service.

***Accommodation.*** Married accommodation available.

***Taxation.*** Income derived by residents of territory from sources within territory is not at present taxable under Commonwealth legislation.

***Further Information.*** An information handbook on the Public Service of the territory and statements on the Department of Public Health and the position of Director are available from the Secretary, Department of Territories, Canberra, A.C.T., Australia, or from the Public Service Board Representative, Australia House, The Strand, London. Other inquiries to Department of Territories, Canberra.

***Applications.*** Applications close with the Secretary, Department of Territories, Canberra, on 31st January, 1958.

## Hospital Services: Non-Medical Appointments

**CHARING CROSS HOSPITAL, W.C.2.** **Part-time** PSYCHIATRIC SOCIAL WORKER required.

Apply in writing to House Governor, stating age, qualifications and experience, with names of 2 referees.

## Miscellaneous

**London Cooperative Society invites applications for** the position of full-time Medical Officer—salary in accordance with qualifications under the recommended British Medical Association scale for Industrial Medical Officers, subject to contract. Contributory superannuation scheme. A medical office will be established in or near the registered offices, 54, Maryland-street, Stratford, London, E.15, but the medical officer will be expected to travel to all parts of the society's trading area. The Medical Officer will be responsible to the Chief Officer and will be required to act in liaison with the staff department (which includes a welfare section).

Applications to be submitted in writing to the Staff Administration Officer at above address, giving details of experience and qualifications, not later than 1 month after the date of this advertisement.

**Medical Officer required by large Oil Company for service** initially based on London but entailing overseas tours of duty and eventually for permanent service in the Middle East. Preference will be given to bachelors under 37 with overseas experience and some knowledge of tropical work. Salary commensurate with qualifications and experience but not less than £1200 p.a. Whilst in U.K. Pension scheme.—Apply, quoting No. 646, to Box No. 1266, c/o CHARLES BARKER & SONS LTD., Gateway House, London, E.C.4.

**Evans Medical Supplies invite applications from medical** practitioners for the post of Head of their Medical Information Department. The post will involve dealing with technical inquiries from doctors and liaison with hospitals, &c., in connection with clinical trials. The post will be based on the Liverpool area. There is a substantial pension and life insurance scheme and the salary will be appropriate to the responsibilities of the post and the qualifications of the successful applicant.—Applications should be made in confidence to the Managing Director of Evans Medical Supplies Limited, Speke, Liverpool 19.

**Korea. Doctor (Female) required with paediatric** experience; age preferably between 26 and 40. Contract 1 year renewable. Salary £1000 p.a. Maintenance equipment allowances and fares paid. 1 month's holiday per year. Duties in Pusan, Korea.

—Apply Foreign Relief Secretary, Save the Children Fund, 12, Upper Belgrave-street, S.W.1. Telephone SLOane 9171.

**Part-time Assistant available, 5 p.m. up to 9 p.m. twice** weekly; occasional weekend or extra work considered. S.W. London preferred. Own car.—Address No. 348, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

**Jewish doctor, well qualified (1952), holding D.C.H.,** seeks good-class partnership or practice in London or South Coast areas. Ample capital available house purchase.—Address No. 347, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

**SWISS PHARMACEUTICAL COMPANY**

of international repute

invites applications from medical men with literary ability for a permanent and pensionable appointment to the staff of the English Section of their

MEDICAL INFORMATION DEPARTMENT

in Basle, Switzerland. This job demands a wide knowledge of all aspects of medico-literary work, and preference will be given to candidates with full- or part-time experience of medical editing and journalism. An M.D. or M.R.C.P. is desirable but not essential providing the candidate is reasonably familiar with contemporary medical practice and literature. An appreciation of the problems of the pharmaceutical industry would also be an advantage. Ability to speak German or French would be useful. The work is varied and interesting and will bring the successful applicant into contact with the pharmacological and clinical research departments. Starting salary will be between Swiss Francs 15,000 and 20,000, depending on experience and qualifications. (Income tax is considerably lower than in the U.K.)

Applications, which will be treated in strict confidence, should give full details. A short list of applicants will be invited for interview in London in the first instance.

Address, No. 341, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

**Charity Commission. In the matter of the Charity** called THE DEVON AND EXETER BENEVOLENT MEDICAL CHARITY, in the County of Devon.

The Charity Commissioners for England and Wales hereby give notice that they propose to establish a Scheme for the regulation of the Charity after the expiration of 1 calendar month.

The Scheme can be seen between the hours of 10 A.M. and 4 P.M. at the offices of Mr. A. Peter Steele-Perkins, Solicitor, at 28, Barnfield-road, Exeter, Devon, and copies can be purchased from the Charity Commission at the price of 4d. each.

Objections or suggestions may be sent within 21 days to the Secretary, Charity Commission, Ryder-street, St. James's, London, S.W.1, quoting the reference E.138391.

2nd November, 1957.

**Consulting room with screening unit in Harley-street/** Wimpole-street area wanted by Cardiologist on a part-time basis. —Address No. 346, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

**Experienced Medical Secretary available 4 mornings** a week, Harley-street area.—HAYWARD, 22, Lymington-road, N.W.6.

**Harley-street area. Use of Consulting-room and facilities,** including radiography, diathermy, &c., available now.—Address, No. 344, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

**Doctors requiring applications, theses copied: Write to** MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC 0141) who are specialists.

**"Pregnancy Diagnosis by the Xenopus Method," 24-hour** service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

**Surgery available in Upper Brook-street, W.1. Modern** attractive building comprising ground and basement floors. Equipped X-ray room. Nominal ground rent. Immediate occupation. £11,000.—Tel. GROsvenor 5292.

**The Disease of Tobacco Smoking and its Cure, by Dr.** Lennox Johnston. 3s. 6d. from all booksellers.—CHRISTOPHER JOHNSON PUBLISHERS LIMITED.

**Typewriting and Duplicating. First-class work at moder-** ate prices by experienced medical typists. Electric machines. —SYBIL RANG, 21, Heath-street, Hampstead, London, N.W.3 (HAM 5329/0504).

**Hypnotism. Will all doctors interested in this subject** for Medical purposes please write to the Secretary, British Society of Medical Hypnotists, 126, Harley-street, W.1.

**Victor fluoroscope, and Cambridge portable E.C.G. for** sale. Also other equipment.—Address, No. 345, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

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# NACTON

## COMPOUND I.S. 499

BENCARD

***a new, long-acting***

**INHIBITOR OF GASTRIC SECRETION**

**which, when given orally, reduces gastric secretion remarkably, and without side-effects in full therapeutic doses**

Nacton promises to be of unusual value in the treatment of peptic ulcer. One dose every six hours provides continuous reduction of acidity.

Previously reported as Compound I.S. 499 (*Brit. med. J.*, ii, 275, 1957), Nacton is now available on National Health Service prescriptions.

**PRESENTATION** *Tablets each containing 2 mg. of (1-methyl-2-pyrrolidyl) methyl benzilate methyl methosulphate. Containers of 50, 250 and 1,000 tablets.*

*LITERATURE AVAILABLE FROM*

**C. L. BENCARD LTD.,** PARK ROYAL, LONDON, N.W.10

601/80/2

# *The new complete treatment for migraine*

# ORGRAINE

| Composition (per tablet) | | Action |
|---|---|---|
| Ergotamine Tartrate B.P. | 1.0 mg. | → constricts dilated cerebral arteries. |
| Caffeine B.P. | 100.0 mg. | → potentiates ergotamine. |
| Hyoscyamine Sulphate B.P.C. (1949) | 0.0875 mg. | → alleviates nausea and vomiting. |
| Atropine Sulphate B.P. | 0.0125 mg. | |
| Phenacetin B.P. | 130.0 mg. | → relieves residual occipital pain. |

In a recent clinical article (J.A.M.A., 1957, 163, 1115) it was stated that in a series of 2,511 cases in which 28 agents were tested in the symptomatic treatment of migraine, ergotamine tartrate was proved to be the most useful drug—and 81% of the patients showed improvement when ergotamine tartrate and caffeine were compounded with belladonna alkaloids. Orgraine applies the same successful principles of treatment.

**PACKS:** Tablets individually foil-stripped, in boxes of 10 and 100.

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